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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

16-August-2001

Subject: ID# 0F06108 - Bifenazate in/on Apple, Apricot, Cotton, Grape, Hops, Nectarine, Peach, Pear, Plum (Prune), and Strawberry. **Evaluation of Residue Data and Analytical Methods.** DP Barcode D277089. Chemical 000586. Case 292702. Submission S575895. MRIDs 44237801, 45052224, 45052225, 45076505, 45052301 - 45052304, 45052311 - 45052328

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Uniroyal Chemical Company, Inc. requested a Section 3 registration for the application of bifenazate to apples, apricots, cotton, grapes, hops, nectarines, peaches, pear, plums (prunes), and strawberries and the establishment of the following permanent tolerances for residues of bifenazate (hydrazinecarboxylic acid, 2-(4-methoxy-[1,1'-biphenyl]-3-yl), 1-methylethyl ester) and D3598 (diazinecarboxylic acid, 2-(4-methoxy-[1,1'-biphenyl]-3-yl), 1-methylethyl ester) expressed as bifenazate:

cottonseed	0.5 ppm
cotton gin byproducts	20 ppm
grapes	0.75 ppm
hops	15 ppm
meat	0.02 ppm
milk	0.01 ppm
pome fruit	0.75 ppm
wet apple pomace	1.2 ppm
stone fruit	1.5 ppm
strawberries	1.5 ppm

BACKGROUND

Bifenazate is a selective miticide which controls the motile stage of mites either by direct contact or through contact with foliar residues. The petitioner indicated that the mode of action of bifenazate is not known. Currently, bifenazate is registered for application to all types of ornamental plants in all areas where these plants grow. HED approved a Section 18 for application of bifenazate to greenhouse grown tomatoes (tolerance of 0.70 ppm; D274300, T. Bloem *et. al.*, 23-May-2001). The current petition is the first Section 3 request for application to a food/feed crop. See attachment 1 for structures of the parent and metabolites.

EXECUTIVE SUMMARY OF CHEMISTRY DEFICIENCIES

- revised Section B (conclusions 2, 9d, and 11)
- revised Section F (conclusions 8b, 9b, 9d, 9h, 9l, 9n, 10c, and 10d)
- petition method validation (PMV) of proposed plant and livestock enforcement methods (conclusions 5b and 5c)
- confirmatory method and interference study for proposed plant and livestock enforcement methods (conclusions 5b and 5c)
- radiovalidation of proposed livestock enforcement method (conclusion 5c)
- FDA multiresidue methods testing of A1530 and A1530-sulfate (conclusion 6)
- storage stability data for hops, strawberry, apple juice, and wet apple pomace (conclusion 7b)
- additional peach field trial data (conclusion 9d)
- additional plum field trial data (conclusion 9d)
- additional grape field trial data (conclusion 9f)
- additional cottonseed field trial data (conclusion 9l)

CONCLUSIONS

OPPTS GLN 830 Series: Product Properties

1. Review of product chemistry data is under the purview of the Registration Division.

OPPTS GLN 860.1200: Directions for Use

2. The petitioner has adequately described the proposed application scenarios. A rotational crop restriction of 30 days for all non-labeled crops should be included on the label. Directions for application to apricots should be removed from the label (see conclusion 9c and 9d). A revised Section B is requested.

OPPTS GLN 860.1300: Nature of the Residue - Plants

3. The HED Metabolism Assessment Review Committee (MARC) reviewed the apple, orange, and cotton metabolism studies and determined that for tolerance expression and risk assessment purposes, the residues of concern in these crops are bifenazate and D3598 (expressed as bifenazate). The metabolic route in apple, orange, and cotton were similar and proceeded via oxidation of the hydrazine moiety of bifenazate to form D3598 which is further degraded to D1989, D9963, D4642, and/or A1530 and to bound residues by reaction with natural products. Since only fruit and oilseed metabolism studies have been submitted, the nature of the residue in all plants is not understood. A metabolism study conducted on a third dissimilar crop (i.e. root/tuber vegetable (root/tuber vegetable in which the leaves are monitored), small grain, Brassica vegetable, or leafy vegetable) is needed prior to drawing conclusions concerning the nature of the residue in all plants (biphenyl hydrazine should be monitored; D276801, T. Bloem, 16-Aug-2001). For the purposes of this petition, HED concludes that the nature of the residue in apple, orange, and cotton are appropriate for translation to pome fruit, nectarine, peach, plum, grape, strawberry, cotton, and hops.

OPPTS GLN 860.1300: Nature of the Residue - Livestock

4. The MARC reviewed the goat and hen metabolism studies and determined that for tolerance expression and risk assessment purposes, the residues of concern in livestock tissue (excluding fat), eggs, and milk are bifenazate, D3598 (expressed as bifenazate), A1530, and A1530-sulfate (expressed as A1530). The residues of concern for tolerance expression and risk assessment purposes in fat are bifenazate and D3598 (expressed as bifenazate). The metabolic route in goats and hens were similar and proceeded via oxidation of the hydrazine moiety of bifenazate to form D3598, loss of the hydrazinecarboxylic acid portion of the molecule, followed by demethylation, hydroxylation, conjugation with glucuronic acid or sulfate, and covalent binding with proteins (D276801, T. Bloem, 16-Aug-2001).

OPPTS GLN 860.1340: Residue Analytical Method

5a. The analytical methods used in the field trial, processing, and ruminant feeding studies were the same as the proposed enforcement methods. The methods have been adequately validated and are appropriate for data gathering purposes. The following paragraphs pertain to the proposed plant and livestock enforcement methods.

5b. *Plant:* The proposed plant enforcement method has been adequately radiovalidated and validated by an independent laboratory. HED forwarded the method to the Analytical Chemistry Laboratory (ACL) for PMV (D271330, T. Bloem, 21-Dec-2000). The petitioner will be required to make any modifications or revisions to the proposed enforcement method resulting from PMV. The petitioner is requested to submit a confirmatory method and an interference study. If the petitioner proposes a confirmatory method which employs a mass selective detector (MSD), then an interference study is not necessary (chromatograms and spectra of fortified samples should be submitted; structurally significant ions should be chosen with a $m/z > 91$ and intensity > 3x noise at the limit of quantitation (LOQ) for the primary method).

5c. *Livestock:* The ILV study resulted in marginal recoveries of bifenazate (milk and kidney), D3598 (liver), and A1530-sulfate (kidney). HED forwarded the method to the ACL for further evaluation and, if appropriate, PMV (D271330, T. Bloem, 21-Dec-2000). The petitioner will be required to make any modifications or revisions to the proposed enforcement method resulting from ACL review and/or PMV. The petitioner is requested to submit radiovalidation of the proposed enforcement method, a confirmatory method, and an interference study. If the petitioner proposes a confirmatory method which employs a MSD, then an interference study is not necessary (chromatograms and spectra of fortified samples should be submitted; structurally significant ions should be chosen with a $m/z > 91$ and intensity > 3x noise at the LOQ for the primary method).

OPPTS GLN 860.1360: Multiresidue Method

6. The petitioner submitted data concerning the recovery of bifenazate and D3598 using FDA multiresidue method protocols A, C, D, E, and F (PAM Vol. I; MRID 45052318). These data were forwarded to FDA for inclusion in the Pesticide Analytical Manual I (D273067, T. Bloem, 6-Mar-2001). The tolerance expression for livestock commodities includes A1530 and A1530-sulfate. The petitioner should submit information concerning the behavior of these compounds through the FDA multiresidue protocols.

OPPTS GLN 860.1380: Storage Stability Data

7a. *Plant:* The storage stability data indicate that residues of bifenazate and D3598 are stable in/on frozen (-20 C) homogenized apple, grape, peach, orange, grape juice, and prunes for 42, 7, 42, 75 (186 days for D3598), 186, and 182 days, respectively. The stability of surface residues was evaluated by fortifying unhomogenized apple, grape, and peach with bifenazate and D3598. The resulting data indicate that surface bifenazate and D3598 residues were stable for 224 days on frozen (-20 C) apple and grape (longest interval tested) but were only stable for 14 days on peach (56 days for bifenazate). The cotton storage stability data indicate that residues of bifenazate and D3598 are stable in frozen (-20 C) cottonseed hulls and oil for 52 and 28 days, respectively (longest interval tested). In cottonseed meal, D3598 was stable for 43 days but bifenazate was not stable for 43 days (43 days was the shortest interval tested for cottonseed meal). Bifenazate and D3598 were not stable for the shortest interval tested in cottonseed (21 days) and cotton gin byproduct (44 days).

7b. HED concludes that the storage intervals for samples collected from all the field trial and processing studies (excluding the apple processing, hop field trial, strawberry field trial, and cotton field trial and processing studies) were validated by the storage stability data. Since none of the currently available data can be translated to hops, HED requests the petitioner to validate the 175 day storage interval for dried hops (7-day interval from homogenization to analysis should also be validated). Since the storage interval for apple juice (295 days) and wet apple pomace (295 days) was greater than any validated interval, HED requests storage stability data for these commodities. Since the surface stability of D3598 on peach was 14 days, HED requests the petitioner to validate the 175 day storage interval for strawberry (5-day interval from homogenization to analysis should also be validated). The maximum interval from harvest or collection to analysis in the cotton field trial and processing studies was 56 days. Since the samples were being harvested on different days and some of the samples had to be sent to a processor, HED concludes that the interval from harvest to analysis was reasonable and will not invalidate the data due to the lack of stability of bifenazate and D3598. However, correction factors of 0.57, 0.60, and 0.70 will be applied to cottonseed, cotton gin byproduct, and cottonseed meal residue data, respectively. The correction factors were based on the average recoveries of bifenazate and D3598 from the storage stability study.

7c. *Livestock:* The storage stability data indicate that residues of bifenazate, D3598, and A1530 were stable in frozen (temperature was not provided) milk and fat for 298 and 95 days, respectively (longest interval tested). Residues of bifenazate and D3598 were not stable in frozen (temperature was not provided) muscle, liver, and kidney as the recoveries dropped below 70% after 2 days of storage (residues of D3598 were stable in muscle for 2 days but not 14 days). Residues of A1530 were stable in frozen (temperature was not provided) muscle, liver, and kidney for 28, 14, and 2 days, respectively. This data validates the storage intervals for the samples collected from the ruminant feeding study.

OPPTS GLN 860.1480: Meat/Milk/Poultry/Eggs

8a. Lactating cows were orally administered bifenazate for 28 consecutive days at feeding levels of 1 ppm (0.2x maximum theoretical dietary burden (MTDB)), 3 ppm (0.5x MTDB), or 10 ppm (1.7x MTDB). Residues of bifenazate/D3598 and A1530/A1530-sulfate were <0.01 ppm in liver, muscle, skim milk, and milk collected from the 10 ppm dosing group. Residues of bifenazate/D3598 were found in butter fat (10 ppm dosing group - 0.01 ppm and 0.03 ppm), kidney (10 ppm dosing group - 0.01 ppm), omental fat (10 ppm dosing group - 0.07 ppm; 3 ppm dosing group - 0.02 ppm), and perirenal fat (10 ppm dosing group - 0.10 ppm; 3 ppm dosing group - 0.03 ppm). Residues of A1530/A1530-sulfate were <0.01 ppm in kidney, butter fat, omental fat, and perirenal fat samples collected from the 10 ppm dosing group. Generally, HED requires a feeding study conducted at 10x the MTDB. For the purposes of this petition, HED will accept the submitted feeding study but advises the petitioner that if the dietary burden increase as a result of additional uses, then a new feeding study may be requested.

8b. Based on the ruminant feeding study and the MTDB for ruminants, HED concludes that the following tolerances for the combined residue of bifenazate, D3598 (expressed as bifenazate), A1530, and A1530-sulfate (expressed as A1530) are appropriate: milk - 0.01 ppm; meat (cattle, goat, hog, horse, and sheep) - 0.01 ppm; meat byproducts (cattle, goat, hog, horse, and sheep) - 0.01 ppm; and fat (cattle, goat, hog, horse, and sheep) - 0.10 ppm (tolerance expression for fat includes only bifenazate and D3598 (expressed as bifenazate)). The petitioner should submit a revised Section F.

8c. Based on the poultry MTDB and the residues identified in the poultry metabolism study, HED concludes that there is no reasonable expectation of finite residues in poultry commodities and will not request a poultry feeding study (category 180.6(a)(3)). The use of the poultry metabolism study in lieu of a feeding study is appropriate for this petition only. If in the future the dietary burden to poultry increases, a poultry feeding study may be required.

OPPTS GLN 860.1500: Crop Field Trials

9a. *Pome Fruit:* The petitioner submitted apple magnitude of the residue data conducted in Region 1 (n=3), Region 2 (n=1), Region 5 (n=1), Region 9 (n=1), Region 10 (n=1), and Region 11 (n=5) and pear magnitude of the residue data conducted in Region 1 (n=2), Region 10 (n=2), and Region 11 (n=4). A single application of a 50WP formulation of bifenazate was applied to apple and pear trees at 1x the maximum proposed seasonal application rate. Apples were harvested 7, 14, and 21 days after application and the combined residues of bifenazate/D3598 ranged from 0.04 - 0.58 ppm, 0.01 - 0.36 ppm, and 0.01 - 0.25 ppm, respectively (7-day preharvest interval requested (PHI)). Pears were harvested 7, 14, and 21 days after application and the combined residues of bifenazate/D3598 ranged from 0.05 - 0.30 ppm, 0.03 - 0.21 ppm, and 0.02 - 0.13 ppm, respectively (7-day PHI requested).

9b. Tables 2 and 5 of OPPTS GLN 860.1500 suggests the following field trial data when requesting a tolerance in/on pome fruit: apple - Region 1 (n=3), Region 2 (n=1), Region 5 (n=2), Region 9 (n=1), Region 10 (n=1), and Region 11 (n=4) and pear - Region 1 (n=1), Region 10 (n=2), and Region 11 (n=3). The geographical distribution of the pear field trial data is adequate. An apple field trial in Region 5 is needed to fulfill the suggested geographical distribution. Since the petitioner conducted an additional apple field trial in Region 11, no additional field trial data will be requested. HED concludes that the available data support the petitioner proposed tolerance of 0.75 ppm for the combined residues of bifenazate and D3598 (expressed as bifenazate) in/on pome fruit. However, the preferred commodity term is "fruit, pome, group." The petitioner should submit a revised Section F.

9c. *Stonefruit:* The petitioner submitted peach magnitude of the residue data conducted in Region 1 (n=1), Region 2 (n=3), Region 5 (n=1), Region 6 (n=1), and Region 10 (n=4) and plum magnitude of the residue data conducted in Region 5 (n=1), Region 10 (n=4), Region 11 (n=1), and Region 12 (n=1). A single application of a 50WP formulation of bifenazate was applied to peach and plum trees at 1x the maximum proposed seasonal application rate. Peaches were harvested 3, 7, and 14 days after application and the combined residues of bifenazate/D3598 ranged from 0.10 - 1.45 ppm, 0.08 - 1.44 ppm, and 0.03 - 0.90 ppm, respectively (3-day PHI requested). Plums were harvested 3, 7, and 14 days after application and the combined residues of bifenazate/D3598 ranged from 0.01 - 0.15 ppm, <0.01 - 0.08 ppm, and <0.01 - 0.05 ppm, respectively (3-day PHI requested).

Tables 2 and 5 of OPPTS GLN 860.1500 suggests the submission of the following field trial data when requesting a tolerance in/on stonefruit: cherry (sweet) - Region 5 (n=2), Region 10 (n=2), and Region 11 (n=2) or cherry (tart) - Region 1 (n=1), Region 5 (n=4), and Region 9 (n=1); peach - Region 1 (n=1), Region 2 (n=3), Region 5 (n=1), Region 6 (n=1), and Region 10 (n=3); and plum - Region 5 (n=1), Region 10 (n=4), and Region 12 (n=1). Since the petitioner has not submitted any cherry field trial data and the maximum peach (1.45 ppm) and plum (0.15 ppm) residue varied by a factor greater than 5x, a stonefruit crop group tolerance is not appropriate and the 25% reduction in the number of field trials when receiving a crop group tolerance does not apply.

9d. Currently, the petitioner is requesting registration for application to peach, nectarine, apricot, and plum. To establish registration on these crops, Table 5 of OPPTS GLN 860.1500 suggests the following geographical field trial distribution: peach - Region 1 (n=1), Region 2 (n=4), Region 4 (n=1), Region 5 (n=1), Region 6 (n=1), and Region 10 (n=4); apricot - Region 10 (n=4) and Region 11 (n=1); and plum - Region 5 (n=1), Region 10 (n=5), Region 11 (n=1), and Region 12 (n=1). The geographical distribution of the field trial data is insufficient and the petitioner should submit the following field trial data: peach - Region 2 (n=1) and Region 4 (n=1); plum - Region 10 (n=1); apricot - Region 10 (n=4) and Region 11 (n=1). Since no apricot field trial data have been submitted, an apricot registration is not appropriate (directions for application to apricots should be removed from the label). Provided the petitioner agrees to submit the requested peach and plum field trial data, HED concludes that the available data support a plum tolerance of 0.30 ppm and a peach tolerance of 1.7 ppm for the combined residue of bifenazate and D3598 (expressed as bifenazate). The petitioner should submit a revised Section F.

9e. *Grape:* The petitioner submitted grape magnitude of the residue data conducted in Region 1 (n=1), Region 10 (n=8), and Region 11 (n=2). A single application of a 50WP formulation of bifenazate was applied to grapes at 1x the maximum proposed seasonal application rate. The grapes were harvested 14 and 21 days after application and the combined residues of bifenazate/D3598 ranged from 0.04 - 0.62 ppm and 0.01 - 0.50 ppm, respectively (14-day PHI requested).

9f. Table 5 of OPPTS GLN 860.1500 suggests the following geographical field trial distribution when requesting a tolerance in/on grapes: Region 1 (n=2), Region 10 (n=8), and Region 11 (n=2). An additional field trial conducted in Region 1 is needed to fulfill the suggested geographical distribution. Provided the petitioner agrees to submit the requested field trial data, HED concludes that the available data support the petitioner proposed tolerance of 0.75 ppm for the combined residue of bifenazate and D3598 (expressed as bifenazate) in/on grape.

9g. *Hops:* The petitioner submitted hop magnitude of the residue data conducted in Region 11 (n=2) and Region 12 (n=1). A single application of a 50WP formulation of bifenazate was applied to hops at 1x the maximum proposed seasonal application rate. The hops were harvested 14 days after application and dried. The combined residues of bifenazate/D3598 ranged from 5.26 - 11.15 ppm.

9h. Table 1 of OPPTS GLN 860.1500 indicates that a minimum of 3 field trials are required for the establishment of a tolerance in/on hops (geographical distribution is not indicated). Table 6 of OPPTS GLN 860.1500 indicated that 94% of the US crop production of hops comes from Region 11. Therefore, the geographical distribution of the hop field trial data is appropriate. Provided the petitioner can validate the 157 day storage interval (7-day interval from homogenization to analysis should also be validated), the submitted field trial data is appropriate and support the petitioner proposed tolerance of 15 ppm for the combined residues of bifenazate and D3598 (expressed as bifenazate) in/on dried hops. However, the preferred commodity term is "hop, dried cone." The petitioner should submit a revised Section F.

9i. *Strawberry:* The petitioner submitted strawberry magnitude of the residue data conducted in Region 1 (n=1), Region 2 (n=1), Region 3 (n=1), Region 5 (n=1), Region 10 (n=3), and Region 12 (n=1). The strawberry plants were treated twice with a 50WP formulation of bifenazate at 1x the maximum proposed single application rate (retreatment interval of 21 or 45 days). The proposed label states that 2 applications are permitted per year with only a single application per harvested crop (retreatment interval of 21 days). Using this treatment scenario, it is likely that early fruiting strawberries may be exposed to two applications of bifenazate and the treatment scenario employed is appropriate for determination of maximum residues. The strawberries were harvested 1 day and 3 days after the second application and the combined residues of bifenazate/D3598 ranged from 0.21 - 1.1 ppm and

0.23 - 3.4 ppm, respectively (1-day PHI requested). The samples harvested 3 days after application from Oceanside, CA resulted in combined bifenazate/D3598 residues of 2.9 and 3.4 ppm. These concentrations are most likely a result of analytical error for the following reasons: **(1)** these values are at least 5x greater then the residues found on the remaining samples harvested 3 days after application, **(2)** the sample collected 1 day after application from this site had a combined bifenazate/D3598 residues of 0.42 ppm and 0.45 ppm, and **(3)** the other sites generally showed a reduction in residues as the pre-harvest interval increased from 1 to 3. Consequently, the samples harvested 3 days after application from Oceanside, CA will not be used when determining the appropriate tolerance. When excluding the Oceanside, CA data the combined residues of bifenazate/D3598 for samples harvested 3 days after application ranged from 0.23 - 0.81 ppm.

9j. Table 5 of OPPTS GLN 860.1500 suggests the following geographical field trial distribution when requesting a tolerance in/on strawberries: Region 1 (n=1), Region 2 (n=1), Region 3 (n=1), Region 5 (n=1), Region 10 (n=3), and Region 11 (n=1). The geographical distribution of the strawberry field trial data is sufficient for registration. Provided the petitioner can validate the 175-day storage interval (5-day interval from homogenization to analysis should also be validated), HED concludes that the available data support the petitioner proposed tolerance of 1.5 ppm for the combined residues of bifenazate and D3598 (expressed as bifenazate) in/on strawberries.

9k. *Cottonseed:* The petitioner submitted cottonseed magnitude of the residue data conducted in Region 2 (n=1), Region 4 (n=3), Region 6 (n=1), Region 8 (n=4), and Region 10 (n=2). A single application of a 50WP formulation of bifenazate was applied to cotton at 1x the maximum proposed seasonal application rate. The cotton was harvested by hand or with mechanical spindle or stripper pickers 60 days after application. The harvested cotton was ginned either at the field site or buy a processor into undelinted cottonseed which was subsequently analyzed. The combined residues of bifenazate/D3598 ranged from <0.02 - 0.54 ppm (residues corrected for loss due to lack of stability; see conclusion 7b).

9l. Table 5 of OPPTS GLN 860.1500 suggests the following geographical distribution when submitting cottonseed residue data: Region 2 (n=1), Region 4 (n=3), Region 6 (n=1), Region 8 (n=4), and Region 10 (n=3). An additional field trial conducted in Region 10 is needed to fulfill the suggested geographical distribution. Provided the petitioner agrees to submit the requested field trial data, HED concludes that the available data support a tolerance of 0.75 ppm for the combined residues of bifenazate and D3598 (expressed as bifenazate) in/on cottonseed. However, the correct commodity definition is "cotton, undelinted seed." A revised Section F should be submitted.

9m. *Cotton Gin Byproduct:* The petitioner submitted cotton gin byproduct magnitude of the residue data conducted in Region 2 (n=1), Region 4 (n=1), Region 8 (n=4), and Region 10 (n=1). A single application of a 50WP formulation of bifenazate was applied to cotton at 1x the maximum proposed seasonal application rate. The cotton was harvested with a mechanical spindle (n=4) or stripper (n=3) pickers 60 days after application. The harvested cotton was ginned by a processor into cotton gin byproduct which was subsequently analyzed. The combined residues of bifenazate/D3598 ranged from 0.10 - 29.17 ppm (residues corrected for loss due to lack of stability; see conclusion 7b).

9n. Table 1 of OPPTS 860.1000 indicates that the petitioner should submit cotton gin byproduct data from a minimum of 6 field trials (3 samples harvested using a stripper and 3 samples harvested using a mechanical picker). The submitted cotton gin byproduct data fulfills the data requirements for cotton gin byproduct. HED concludes that the available data support a tolerance of 35 ppm for the combined residues of bifenazate and D3598 (expressed as bifenazate) in/on cotton, gin byproducts. A revised Section F should be submitted.

OPPTS GLN 860.1520: Processed Food/Feed

10a. *Cotton:* A single application of a 50WP formulation of bifenazate was applied to cotton at 6x the maximum proposed seasonal application rate. The cotton was harvested 60 days after application and processed into seed, hulls, meal, and refined oil. The resulting data indicate that the combined residues of bifenazate/D3598 reduced as the cottonseed was processed into hulls (0.2x), meal (<0.01x), and refined oil (<0.01x). Therefore, tolerances for the processed commodities will be covered by the raw agricultural commodity (RAC).

10b. *Plum:* A single application of a 50WP formulation of bifenazate was applied to plum trees at 1x the maximum proposed seasonal application rate. Plums were harvested 3 days after application and processed into prunes. The resulting data indicated that the combined residues of bifenazate/D3598 reduced as the plums were processed to prunes (0.5x). Therefore, tolerances for the processed commodities will be covered by the RAC.

10c. *Apple:* A single application of a 50WP formulation of bifenazate was applied to apple trees at 5x the maximum proposed seasonal application rate. Apples were harvested 7 days after application and processed into juice and wet pomace. The resulting data indicate that the combined residues of bifenazate/D3598 reduced in apple juice (0.23x) but concentrated in wet apple pomace (1.82x). The highest average field trial (HAFT) for apples was 0.58 ppm. Provided the petitioner can validate the 295-day storage interval for apple juice and wet apple pomace, HED concludes that an apple juice tolerance is unnecessary and the petitioner proposed tolerance for the combined residues of bifenazate and D3598 (expressed as bifenazate) in/on wet apple pomace of 1.2 ppm is appropriate (HAFT x processing factor = 0.58 x 1.82 = 1.1 ppm). However, the preferred commodity term is "apple, wet pomace." A revised Section F should be submitted.

10d. *Grape:* A single application of a 50WP formulation of bifenazate was applied to grape vines at 5x the maximum proposed seasonal application rate. Grapes were harvested 14 days after application and processed into juice and raisins and the samples were analyzed for bifenazate/D3598. The resulting data indicate that the combined residues of bifenazate/D3598 reduced in grape juice (0.17x) but concentrated in raisin (2.06x). The HAFT for grapes was 0.55 ppm. HED concludes that a grape juice tolerance is unnecessary and a tolerance for the combined residues of bifenazate and D3598 (expressed as bifenazate) in/on raisin of 1.2 ppm is appropriate (HAFT x processing factor = 0.55 x 2.06 = 1.1). The preferred commodity term is "grape, raisin." A revised Section F should be submitted.

OPPTS GLN 860.1850: Confined Accumulation in Rotational Crops

11. The MARC reviewed the confined rotational crop study and concluded that residues of concern in/on rotational crops could not be determined from the available data (D276801, T. Bloem, 16-Aug-2001). Provided the petitioner includes a 30-day rotational crop restriction for all non-labeled crops, HED concludes that tolerances for rotational crops are not necessary for the following reasons (a revised Section B should be submitted): (1) total radioactive residues (TRR) in mature carrot planted 30 days after treatment were <0.01 ppm (0.007 ppm); (2) TRR in mature lettuce planted 30 days after treatment were 0.014 ppm. However upon analysis no residue >0.01 ppm could be identified; and (3) TRR in and 30-day wheat forage, wheat hay, wheat chaff, and wheat grain were 0.038 ppm, 0.117 ppm, 0.031 ppm, and 0.016 ppm, respectively. However, upon analysis no residues >0.01 ppm could be identified.

International Harmonization

12. There is neither a Codex proposal, nor Canadian or Mexican limits, for residues of bifenazate and D3598 in/on pome fruit, stonefruit, strawberry, hops, cotton, or grape or for residues of bifenazate, D3598, A1530 and A1530-sulfate in/on livestock commodities (see attachment 1). Therefore harmonization is not an issue for this petition.

RECOMMENDATIONS

HED concludes that the residue chemistry database does not support registration for application of bifenazate to apricots (see conclusions 9c and 9d). Provided the petitioner addresses the deficiencies identified in conclusions 2, 5b, 5c, 6, 8b, 9b, 9d, 9f, 9h, 9l, 9n, 10c, 10d, and 11, HED concludes that the residue chemistry database supports conditional registration and establishment of the permanent tolerances listed below. The tolerance expression for plants and for livestock fat tissue is for the combined residues of bifenazate (hydrazinecarboxylic acid, 2-(4-methoxy-[1,1'-biphenyl]-3-yl), 1-methylethyl ester) and D3598 (expressed as bifenazate; diazinecarboxylic acid, 2-(4-methoxy-[1,1'-biphenyl]-3-yl), 1-methylethyl ester) and the tolerance expression for livestock commodities (excluding fat) is for the combined residues of bifenazate (hydrazinecarboxylic acid, 2-(4-methoxy-[1,1'-biphenyl]-3-yl), 1-methylethyl ester), D3598 (expressed as bifenazate; diazinecarboxylic acid, 2-(4-methoxy-[1,1'-biphenyl]-3-yl), 1-methylethyl ester), A1530 (1,1'-biphenyl, 4-ol), and A1530-sulfate (expressed as A1530; 1,1'-biphenyl, 4-oxysulfonic acid).

cotton, undelinted seed	0.75 ppm
cotton, gin byproducts	35 ppm
grape	0.75 ppm
grape, raisin	1.2 ppm
hop, dried cones	15 ppm
fruit, pome, group	0.75 ppm
apple, wet pomace	1.2 ppm
peach	1.7 ppm
plum	0.30 ppm
strawberry	1.5 ppm
*fat	0.10 ppm
*meat	0.01 ppm
*meat byproducts	0.01 ppm
milk	0.01 ppm

* cattle, goat, hog, horse, and sheep

DETAILED CONSIDERATIONS

OPPTS GLN 830 Series: Product Properties

Review of product chemistry data is under the purview of the Registration Division.

OPPTS GLN 860.1200: Directions for Use

The petitioner is proposing application of Acramite™ (50% bifenazate; wettable powder (WP) formulation in water soluble bags) to apples, apricots, cotton, grapes, hops, nectarines, peaches, pear, plums (prunes), and strawberries for the control of mites. Application through any type of irrigation system is prohibited. The label indicates that coverage is improved when an organosilicone surfactant is added to the tank mixture. The following is a summary of the proposed application scenarios.

apple: A single application per year is proposed at 0.25 - 0.50 lbs ai/acre. The product is to be applied in a minimum of 50 gallons of water/acre. Harvest is not permitted within 7 days of application.

apricot: A single application per year is proposed at 0.25 - 0.50 lbs ai/acre. The product is to be applied in a minimum of 50 gallons of water/acre. Harvest is not permitted within 3 days of application.

cotton: A single application per year is proposed at 0.25 - 0.75 lbs ai/acre. The product is to be applied in a minimum of 20 gallons of water/acre. Harvest is not permitted within 60 days of application.

grape: A single application per year is proposed at 0.25 - 0.50 lbs ai/acre. The product is to be applied in a minimum of 50 gallons of water/acre. Harvest is not permitted within 14 days of application.

hops: A single application per year is proposed at 0.25 - 0.75 lbs ai/acre. The product is to be applied in a minimum of 50 gallons of water/acre. Harvest is not permitted within 14 days of application.

nectarine: A single application per year is proposed at 0.25 - 0.50 lbs ai/acre. The product is to be applied in a minimum of 50 gallons of water/acre. Harvest is not permitted within 3 days of application.

peach: A single application per year is proposed at 0.25 - 0.50 lbs ai/acre. The product is to be applied in a minimum of 50 gallons of water/acre. Harvest is not permitted within 3 days of application.

pear: A single application per year is proposed at 0.25 - 0.50 lbs ai/acre. The product is to be applied in a minimum of 50 gallons of water/acre. Harvest is not permitted within 7 days of application.

plums (prunes): A single application per year is proposed at 0.25 - 0.50 lbs ai/acre. The product is to be applied in a minimum of 50 gallons of water/acre. Harvest is not permitted within 3 days of application.

strawberry: Two applications per year are proposed with only a single application per harvested crop at 0.25 - 0.50 lbs ai/acre. Minimum period between applications is 21 days. The product is to be applied in a minimum of 100 gallons of water/acre. Harvest is not permitted within 1 day of application.

Conclusions: The petitioner has adequately described the proposed application scenarios. A rotational crop restriction of 30 days for all non-labeled crops should be included on the label. Directions for application to apricots should be removed from the label. A revised Section B is requested.

OPPTS GLN 860.1300: Nature of the Residue Plants

MRID 442378-01: Metabolism of [^{14}C]D2341 in Apples: The in-life phase of the study was conducted by Research for Hire, Inc (Porterville, CA) and the analytical phase of the study was conducted by Ricerca Inc. (Painesville, OH). [^{14}C]Bifenazate (252,000dpm/µg; ≥98% radiochemical purity; substituted phenyl ring labeled) was mixed with unlabeled bifenazate (final activity of 86,829 dpm/µg), added to a formulation blank, mixed with water, and applied to Granny Smith apple trees at 0.375 lbs ai/acre (0.75x the maximum proposed single and seasonal application rate) or 2.0 lbs ai/acre (4x the maximum proposed single and seasonal application rate). Applications were performed with broadcast spray equipment. Leaf samples were collected 0 and 101 days after treatment (DAT) and placed in a freezer within 1 hour of collection. Mature apples were harvested from all plots 101 DAT and placed in a refrigerator within 1 hour of collection. All samples were shipped frozen or refrigerated to the analytical laboratory within 4 days of collection. Upon arrival at the analytical laboratory, the samples were immediately processed and analyzed for TRR. Table 1 is a summary of the TRR found in the harvested samples.

Table 1: TRR

matrix (DAT)	ppm bifenazate equivalents	
	0.375 lbs ai/acre	2.0 lbs ai/acre
leaf (0)	60.0	310.5
leaf (110)	9.3	70.8
apple fruit (110)	0.088	0.373

Extraction and Characterization of Residues: The following procedures were performed on mature apple fruit from both application scenarios. The resulting distribution/identification of residues from each application scenario were similar and only the results from the samples treated at the exaggerated rate will be presented.

The apple fruit samples were washed with acetonitrile (ACN; 66% TRR), homogenized, and the homogenate separated into solid (pomace; 26% TRR) and aqueous fraction (juice; 9% TRR). The pomace was extracted with ACN (0.1% acetic acid; 7% TRR) followed by ACN:water (50:50, 0.1% acetic acid; 4% TRR). The postextraction solids (PES; 14% TRR) were hydrolyzed with 1.0N HCl (1% TRR), 1.0N NaOH (10% TRR), cellulase (1% TRR), hemicellulase (2% TRR), Pectinex® (2% TRR), and β-glucosidase (1% TRR). The base hydrolysate was partitioned with ethyl acetate at acidic and basic pH and the ethyl acetate phases were combined (8% TRR).

Instrumental Analysis: The ACN wash, ACN extract, ACN/water extract, aqueous phase (juice), hemicellulase hydrolysate, and ethyl acetate fractions of the base hydrolysate were HPLC analyzed. Residues were identified by cochromatography with the following standards: bifenazate, D3598, D1989, D4111, D4274, D4642, D6887, D9472, D9569, D9963, A1530, C8932, and C8935. The HPLC effluent was monitored by an in-line radioactivity flow detector and quantitation was by fraction collection followed by LSC analysis (LOQ = 0.001 ppm). Identified residues were confirmed via TLC analysis or by mass spectral comparison with standards. Table 2 is a summary of the characterization/identification of TRR in apple fruit.

The initial HPLC analysis of the ACN wash, ACN extract, and ACN/water extract and the analysis of the aqueous fraction (juice) resulted in regions which showed numerous minor components and/or broad unresolved radioactivity. The TRR in these regions were ≤5% for all regions excluding the 2-8.5 minute region (22% TRR). D9472 eluted in the 2-8.5 minute region and could not be excluded as a possible metabolite. Based on the retention time of the standard, the petitioner estimated that D9472 could be present at 0.002 ppm (0.6% TRR). In an attempt to better characterize the radioactivity in this region, the petitioner isolated the 2-8.5 minute region from a leaf extract and subjected the collected material to acid, base, and β-glucosidase hydrolysis followed by HPLC analysis. β-glucosidase hydrolysis did not release any major peaks. Acid and base hydrolysis gave a peak eluting at 15 minutes which was isolated and analyzed via LC/MS (spectrum did not correspond to any available bifenazate metabolites; M/Z of 346).

Storage Stability: The petitioner indicated that the samples were stored at <-5 C prior to extraction and were analyzed within 30 days of harvest. Juice and pomace samples from apples which had been stored for 6 months were extracted as described above. The resulting data was compared to the initial analysis and demonstrated that residues of bifenazate are fairly stable in apple matrices when stored frozen. Since the samples were analyzed within 30 days of harvest, the submitted storage stability data is sufficient to validate this study.

Apple Metabolism Summary: TRR in mature apples harvested 101 DAT with [^{14}C]bifenazate (substituted phenyl ring labeled) at 2.0 lbs ai/acre (4x the proposed seasonal rate) were 0.373 ppm. A surface ACN wash of the harvested fruit removed 66% of the TRR and consisted largely of bifenazate (46% TRR). The washed fruit was homogenized and the solid material (pomace; 26% TRR) was separated from the aqueous fraction (juice; 9% TRR). HPLC analysis of juice resulted in the majority of the radioactivity eluting as diffuse radioactivity in the 2-8.5 minute region (polar; 8% TRR). Analysis of the material extractable from pomace resulted in the identification of bifenazate (0.4% TRR) and diffuse radioactivity eluting in the 2-8.5 minute region (polar; 8% TRR). PES represented 14% of the TRR; the majority of which was characterized as organosoluble (8% TRR) after base hydrolysis. The petitioner proposed metabolic pathway indicates that bifenazate is initially oxidized to D3598 which is further degraded to D1989, D4642, and bound residues by reaction with natural products (see attachment 2).

Table 2: Distribution/Identification of TRR in Mature Apple Fruit Harvested 101 DAT with [^{14}C]-Bifenazate at 2.0 lbs ai/acre (4x the maximum proposed seasonal rate)

	ppm (% TRR)[1]			
	total	**ACN surface wash**	**pomace (solids)**	**juice (aq. fraction)**
total	**0.373**	**0.244 (65.5%)**	**0.096 (25.7%)**	**0.033 (8.9%)**
extractable	0.316 (84.7%)	0.244 (65.5%)	0.038 (10.3%)[2]	0.033 (8.9%)
bifenazate[3]	0.175 (46.9%)	0.173 (46.5%)	0.001 (0.4%)	<0.001 (<0.1%)
D3598[3]	0.017 (4.5%)	0.015 (4.1%)	0.001 (0.3%)	<0.001 (0.1%)
D4642[4]	0.003 (0.8%)	0.003 (0.7%)	<0.001 (<0.1%)	<0.001 (0.1%)
D1989[4]	0.001 (0.2%)	0.001 (0.2%)	<0.001 (<0.1%)	<0.001 (<0.1%)
D6887[3]	0.001 (0.3%)	<0.001 (0.1%)	<0.001 (0.1%)	<0.001 (0.1%)
unknown 1[5]	<0.001 (0.1%)	<0.001 (0.1%)	<0.001 (<0.1%)	<0.001 (<0.1%)
region 2-8.5 min[6]	0.082 (22.0%)	0.021 (5.5%)	0.031 (8.3%)	0.031 (8.2%)
region 8.5-13 min	0.018 (4.7%)	0.015 (4.0%)	0.002 (0.6%)	<0.001 (0.1%)
region 14.5-18 min	0.019 (5.1%)	0.018 (4.7%)	0.001 (0.3%)	<0.001 (0.1%)
region 19.5-25 min	0.005 (1.4%)	0.003 (0.7%)	0.001 (0.3%)	0.001 (0.4%)
PES[7]	0.053 (14.1%)	--	0.053 (14.1%)	--
cellulase	0.004 (1.2%)	--	0.004 (1.2%)	--
hemicellulase	0.007 (1.9%)	--	0.007 (1.9%)	--
Pectinex®	0.007 (1.7%)	--	0.007 (1.7%)	--
β-glucosidase	0.003 (0.8%)	--	0.003 (0.8%)	--
total identified	**0.197 (52.8%)**	**0.192 (51.6%)**	**0.002 (0.6%)**	**<0.001 (0.2%)**

1 bifenazate equivalents; ACN washed fruit was homogenized and separated into pomace and juice
2 0.025 ppm (6.7% TRR) ACN extractable and 0.013 ppm (3.6% TRR) ACN/water extractable
3 confirmed by MS analysis
4 confirmed by TLC analysis
5 molecular peak at m/z of 400
6 composed of several peaks ≤0.028 ppm (≤7.4% TRR); D9472 eluted in this region and based on the retention time the petitioner estimated that D9472 could be present at 0.002 ppm (0.6% TRR)
7 aliquots of apple pomace PES were hydrolyzed with the enzymes listed

MRID 45052312: Metabolism of [^{14}C]D2341 in Citrus: The in-life phase of the study was conducted by Plant Sciences, Inc (Watsonville, CA) and the analytical phase of the study was conducted by Ricerca Inc. (Painesville, OH). [^{14}C]Bifenazate (254,000dpm/µg; ≥98% radiochemical purity; substituted phenyl ring labeled) was mixed with unlabeled bifenazate (final activity of 68,447 dpm/µg), added to a formulation blank, mixed with water, and applied to dwarf Valencia orange trees at 0.375 lbs ai/acre or 2.0 lbs ai/acre. Applications were performed with broadcast spray equipment. Leaf samples were collected 0, 43, and 184 DAT; placed in a freezer; and shipped to the analytical laboratory within 7 days of harvest. Mature oranges were collected 43, 184, 274, and 442 DAT; placed in a cooler along with ice packs; and shipped on the day of collection to the analytical laboratory. Upon arrival at the analytical laboratory, the samples were immediately processed and analyzed for TRR. Table 3 is a summary of the TRR found in the harvested samples.

Table 3: TRR

matrix (DAT)	ppm bifenazate equivalents	
	0.375 lbs ai/acre	2.0 lbs ai/acre
leaf (0)	27.6	110.3
leaf (43)	20.6	89.5
leaf (184)	5.4	23.9
orange fruit (43)	0.353	1.466
orange fruit (184)	0.096	na
orange fruit (274)	0.095	0.081
orange fruit (442)	0.013	0.032

Extraction and Characterization of Residues: The following procedures were performed on orange fruit collected 43 DAT collected from both application scenarios. The resulting distribution/identification of residues from each application scenario were similar and only the results from the samples treated at 2.0 lbs ai/acre will be presented.

The orange fruit samples (43 DAT; 1.466 ppm) were washed with ACN (81% TRR). The washed fruit was peeled (18% TRR) and the peeled fruit was processed into juice (1% TRR) and pulp (1% TRR). Peel and pulp were extracted with ACN (0.1% acetic acid; peel - 10% TRR; pulp - 0.4% TRR) followed by ACN:water (50:50, 0.1% acetic acid; peel - 3% TRR; pulp - 0.2% TRR). Juice was extracted with ACN (0.6% TRR). The PES from pulp (0.3% TRR) and juice (0.2% TRR) were not analyzed further. The PES from peel (5% TRR) were hydrolyzed with 3.0N HCl (4% TRR) and the hydrolysate was partitioned with methylene chloride (methylene chloride - 2% TRR; aqueous phase - 1% TRR).

Instrumental Analysis: The ACN wash, ACN extracts, ACN/water extracts, and the methylene chloride partitions of the acid hydrolysate of peel were HPLC analyzed. Residues were identified by cochromatography with the following standards: bifenazate, D3598, D1989, D4642, D9472, and D9963. The HPLC effluent was monitored by an in-line radioactivity flow detector and quantitation was by fraction collection followed by LSC analysis (LOQ = 0.001 ppm). Residues of bifenazate and D3598 were confirmed via TLC analysis or by mass spectral comparison with standards.

The initial HPLC analysis of the ACN and ACN/water extracts of peel, pulp, and juice resulted in a region (2-5 minutes) of broad unresolved radioactivity. This region of radioactivity was isolated from the peel extract and analyzed using a different HPLC system. The analysis showed the presence of a number of radioactive components each <1% TRR. D9472 eluted in the 2-5 minute region and could not be excluded as a possible metabolite. Based on the retention time of the standard, the petitioner estimated that D9472 could be present at 0.002 ppm (0.1% TRR). The isolated region was also subjected to acid, base, and β-glucosidase hydrolysis. HPLC analysis of the resulting hydrolysates showed numerous radioactive components with no single major residue.

Storage Stability: The petitioner indicated that the samples were stored at <-5 C prior to analysis and were analyzed within 30 days of harvest. Juice, pulp, and peel samples that had been stored for 14 months were extracted and analyzed as described above. The resulting data was compared to the initial analysis and variation in the %TRR for D3598 (juice and pulp), D4642/D1989 (juice), and the polar region (pulp) were noted. Since the samples were analyzed within 30 days of harvest, the submitted storage stability data is sufficient to validate this study.

Table 4: Distribution/Identification of TRR in Orange Fruit Harvested 43 DAT with [^{14}C]-Bifenazate at 2.0 lbs ai/acre

	ppm (% TRR)[1]				
	total	**ACN surface wash**	**peel**	**pulp**	**juice**
total	**1.466**	**1.182 (80.2%)**	**0.259 (17.7%)**	**0.013 (0.9%)**	**0.012 (0.8%)**
extractable	1.384 (94.4%)	1.182 (80.2%)	0.185 (12.6%)[2]	0.009 (0.6%)[3]	0.009 (0.6%)
bifenazate[4]	1.161 (79.2%)	1.121 (76.5%)	0.037 (2.5%)	0.001 (0.1%)	0.001 (0.1%)
D3598[4]	0.088 (6.0%)	0.060 (4.1%)	0.028 (1.9%)	<0.001 (<0.1%)	<0.001 (<0.1%)
D4642	0.004 (0.3%)	<0.001 (<0.1%)	0.004 (0.3%)	<0.001 (<0.1%)	<0.001 (<0.1%)
D1989	0.003 (0.2%)	<0.001 (<0.1%)	0.003 (0.2%)	<0.001 (<0.1%)	<0.001 (<0.1%)
D9963	0.012 (0.8%)	<0.001 (<0.1%)	0.012 (0.8%)	<0.001 (<0.1%)	<0.001 (<0.1%)
polar region[5]	0.086 (5.9%)	<0.001 (<0.1%)	0.075 (5.1%)	0.006 (0.4%)	0.006 (0.4%)
PES	0.082 (5.6%)	<0.001 (<0.1%)	0.075 (5.1%)	0.004 (0.3%)	0.003 (0.2%)
total identified	**1.268 (86.5%)**	**1.181 (80.6%)**	**0.084 (5.7%)**	**0.001 (0.1%)**	**0.001 (0.1%)**

[1] bifenazate equivalents; ACN washed fruit was peeled and the peeled fruit was processed into juice and pulp; peel and pulp were extracted with ACN (0.1% acetic acid) followed by ACN:water (50:50, 0.1% acetic acid); juice was only extracted with ACN.

[2] 0.147 ppm (10.0% TRR) ACN extractable and 0.038 ppm (2.6% TRR) ACN/water extractable

[3] 0.006 ppm (0.4% TRR) ACN extractable and 0.003 ppm (0.2% TRR) ACN/water extractable

[4] confirmed by MS analysis

[5] composed of several peaks <1% TRR; D9472 eluted in this region and based on the retention time the petitioner estimated that D9472 could be present at 0.002 ppm (0.1% TRR)

Orange Metabolism Summary: TRR in mature orange fruit harvested 43 DAT with [^{14}C]bifenazate (substituted phenyl ring labeled) at 2.0 lbs ai/acre were 1.446 ppm. A surface ACN wash of the harvested fruit removed 81% of the TRR and consisted largely of bifenazate (76% TRR). The ACN washed fruit was peeled (18% TRR) and the peeled fruit separated into juice (1% TRR) and pulp (1% TRR). The major residue identified in peel, pulp, and juice was bifenazate (total of 3% TRR) with minor ammounts of D3598, D4642, D1989, and D9963 also identified. The petitioner proposed metabolic pathway indicates that bifenazate is initially oxidized to D3598 which is further degraded to D1989, D9963, and bound residues by reaction with natural products (see attachment 3).

MRID 45052313: Metabolism of [^{14}C]D2341 in Cotton: The in-life phase of the study was conducted by Research For Hire, Inc (Porterville, CA) and the analytical phase of the study was conducted by Ricerca Inc. (Painesville, OH). [^{14}C]Bifenazate (246,149 dpm/µg; >98% radiochemical purity; substituted phenyl ring labeled) was mixed with unlabeled bifenazate (final activity of 88,500 dpm/µg), added to a formulation blank, mixed with water, and applied to cotton at 0.5 lbs ai/acre or 2.0 lbs ai/acre (0.7x and 2.7x the maximum proposed seasonal application rate). The mature cotton was harvested 112 DAT. The cotton was mechanically ginned and the resulting seed samples were collected. The cotton plants were also harvested for cotton gin byproducts by collecting leaves, petioles, calyx, and unopened immature bolls. The cotton gin byproduct material was dried overnight under heat lamps and small portions were placed in a coffee grinder and ground. Cottonseed samples were placed in frozen storage (-20 C) within 3 hours of collection and cotton gin byproduct samples were handled as described above and then placed in frozen storage. The samples were shipped frozen to the analytical laboratory via overnight delivery. Table 5 is a summary of the TRR found in the harvested samples.

Table 5: TRR

	ppm bifenazate equivalents	
	0.5 lbs ai/acre	**2.0 lbs ai/acre**
cottonseed	0.075	0.125
cotton gin byproduct	0.410	0.838

Extraction and Characterization of Residues: The following procedures were performed on cottonseed and cotton gin byproducts samples collected from both application scenarios. The resulting distribution/identification of residues from each application scenario were similar and only the results from the samples treated at 2.0 lbs ai/acre will be presented.

Cottonseed (0.125 ppm): A seed sample was homogenized with hexane (23% TRR) and ACN:water (50:50, 0.1% acetic acid; 14% TRR). The hexane fraction was concentrated, saponified with 0.3N NaOH in 90% aqueous methanol, and partitioned with hexane (hexane - 21% TRR; aqueous - 5% TRR, not further analyzed). The PES (63% TRR) were analyzed via four procedures which are summarized below: **(1)** A sub-sample of the PES were mixed with a 5% dodecylsulfate (SDS) and 25 mM dithiothreitol (solublizes proteins and reduces disulfide bonds in proteins; 50 C for 16 hours). The hydrolysate (24% TRR) was separated from the unextracted material (39% TRR) and analyzed using gel permeation chromatography (GPC). The majority of the hydrolyzed radioactivity was determined to be high molecular weight compounds which were collected and treated with a protease (38 C, 16 hours). The resulting hydrolysate was GPC analyzed and indicated that the protease treatment converted some of the high molecular weight material to low molecular weight. The solid material (39% TRR) remaining after SDS treatment was refluxed with 1N sulfuric acid for 4 hours and the hydrolysate (12% TRR) was separated from the remaining solids (31% TRR); **(2)** A sub-sample of the PES were sequentially hydrolyzed with protease (37 C, 24 hours; 25% TRR), 72% sulfuric acid (room temperature, 3 hours; 12% TRR), and 1N NaOH (40 C, 16 hours; 2% TRR). The remaining solid material (13% TRR) was not further analyzed; **(3)** A sub-sample of the PES were sequentially hydrolyzed with methanol:water:HCl (50:50:1; 6% TRR) and 1N HCl in 50% aqueous methanol (room temp, 16 hours; 2% TRR). The remaining solid material (54% TRR) was not further analyzed; and **(4)** A sub-sample of the unextracted material was hydrolyzed with with methanol:water:HCl (50:50:1) using a probe sonicator for 10 minutes. The extraction mixture was centrifuged and the supernatant (3% TRR) was separated from the solid material (64% TRR).

Cotton Gin Byproduct (0.838 ppm): A gin byproduct sample was homogenized with ACN (0.1% acetic acid; 56% TRR) and ACN:water (50:50, 0.1% acetic acid; 26% TRR). The PES (34% TRR) were analyzed via four procedures which are summarized below: **(1)** A sub-sample of the PES were sequentially hydrolyzed with cellulase (37 C, 24 hours; 6 % TRR) and hemicellulase (37 C, 24 hours; 3% TRR). The remaining solid material (27% TRR) was not further analyzed; **(2)** A sub-sample of the PES were sequentially hydrolyzed with 72 % sulfuric acid (room temp, 3 hours; 12% TRR) and 1N NaOH (40 C, 16 hours 1% TRR). The remaining solid material (14% TRR) was not further analyzed; **(3)** A sub-sample of the PES were extracted with hexane (1% TRR) and sequentially hydrolyzed with methanol:water:HCl (50:50:1; 8% TRR) and 1N HCl in 50% aqueous methanol (room temp, 16 hours; 1% TRR). The remaining solid material (24% TRR) was not further analyzed; and **(4)** A sub-sample of the PES were hydrolyzed with methanol:water:HCl (50:50:1) using a probe sonicator for 10 minutes. The hydrolysate (3% TRR) was separated from the solid material (33% TRR).

Instrumental Analysis: All hexane, ACN, and aqueous ACN extracts were HPLC analyzed. Residues were identified by cochromatography with the following standards: bifenazate, D3598, D4111, D1989, D4642, D4274, A1530, D9472, I0199, and D9477. The HPLC effluent was monitored by an in-line radioactivity flow detector and quantitation was by fraction collection followed by LSC analysis (LOQ = 0.001 ppm). Residues identified in cotton gin byproduct were confirmed via TLC analysis or by mass spectral comparison with standards (residues in cottonseed where to low for confirmation).

The initial HPLC analysis of the hexane, ACN, and/or aqueous ACN extracts resulted in broad unresolved regions of radioactivity eluting in the following regions: 2-6 minutes (seed and gin byproduct), 19-26 minutes (gin byproduct), 26-29 minutes (gin byproduct), and 29-33 minutes (gin byproduct). These regions were isolated and subjected to various hydrolysis procedures. The isolated 2-6 minute region of the seed extract was subjected to mild acid and mild base hydrolysis and the isolated 2-6 minute region of cotton gin byproduct extract was subjected to mild acid, mild base, and strong acid hydrolysis. The hydrolysates were HPLC analyzed and the resulting chromatograms were not significantly different from the unhydrolyzed extracts. The isolated 19-26, 26-29, and 29-33 minute regions of cotton gin byproduct were subjected to hydrolysis with mild acid, mild base, strong acid, and β-glucosidase. The resulting chromatograms were not significantly different from the unhydrolyzed sample except for the strong acid hydrolysate from the 26-29 minute region which resulted in the identification of A1530 and D9963 (confirmed via TLC analysis).

The hexane extractable fraction of cottonseed was HPLC analyzed and nearly all of the radioactivity eluted at ~40 minutes (non-polar). The hexane extract was saponified and the resulting extract partitioned with hexane. The hexane partition was HPLC analyzed and resulted in peaks with nearly identical retention times to linoleic acid, palmitic acid, and oleic acid (quantitative data was not provided).

Storage Stability: The petitioner indicated that the samples were stored at <-5 C prior to analysis and were analyzed within 30 days of harvest. Cotton gin byproducts that had been stored for 7 months were extracted and analyzed as described above. The resulting data was compared to the initial analysis and demonstrated that bifenazate residues were stable in/on cotton gin byproduct. No storage stability data for cottonseed was submitted with this study. Since the samples were analyzed within 30 days of harvest, the submitted storage stability data is sufficient to validate this study.

Table 6: Distribution/Identification of TRR in Cottonseed and Cotton Gin Byproduct Harvested 112 DAT with [^{14}C]-Bifenazate at 2.0 lbs ai/acre (2.7x the maximum proposed seasonal rate)

	ppm bifenazate equivalents (% TRR)		
	total	**hexane extract**	**50% ACN extract**
cottonseed total	**0.125**	**0.028 (22.7%)**	**0.018 (14.5%)**
bifenazate	<0.001 (<0.1%)	<0.001 (<0.1%)	<0.001 (<0.1%)
D3598	<0.001 (<0.1%)	<0.001 (<0.1%)	<0.001 (<0.1%)
D4642/D1989	<0.001 (<0.1%)	nd	<0.001 (<0.1%)
2-6 minute region[1]	0.018 (14.4%)	nd	0.018 (14.4%)
6-13 minute region[2]	0.004 (2.9%)	nd	0.004 (2.9%)
40 minute region[3]	0.028 (22.7%)	0.028 (22.7%)	nd
unextracted[4]	0.079 (62.8%)	--	--
protease	0.032 (25.3%)	--	--
sulfuric acid	0.015 (11.6%)	--	--
NaOH	0.003 (2.3%)	--	--
PES	0.017 (13.2%)	--	--
total identified	**<0.001 (<0.1%)**	**<0.001 (<0.1%)**	**<0.001 (<0.1%)**
	ppm bifenazate equivalents (% TRR)[1]		
	total	**ACN extract**	**50% ACN extract**
gin byproduct; total	**0.838**	**0.465 (55.5%)**	**0.220 (26.3%)**
bifenazate[5]	0.338 (40.3%)	0.006 (0.7%)	0.332 (39.6%)
D3598[5]	0.051 (6.1%)	0.001 (0.1%)	0.050 (6.0%)
D1989[6]	0.009 (1.1%)	<0.001 (<0.1%)	0.009 (1.1%)
D4642[6]	0.004 (0.5%)	<0.001 (<0.1%)	0.004 (0.5%)
A1530[6]	0.015 (1.8%)	nd	0.015 (1.8%)
D9963[6]	0.007 (0.8%)	nd	0.007 (0.8%)
2-6 minute region[1]	0.061 (7.3%)	nd	0.061 (7.3%)
6-13 minute region[2]	0.045 (5.4%)	nd	0.045 (5.4%)
19-26 minute region[7]	0.051 (6.1%)	nd	0.051 (6.1%)
26-29 minute region[7]	0.029 (3.5%)	nd	0.029 (3.5%)
29-33 minute region[7]	0.026 (3.1%)	nd	0.026 (3.1%)
unextracted	0.288 (34.4%)	--	--

	ppm bifenazate equivalents (% TRR)[1]		
	total	ACN extract	50% ACN extract
cellulase	0.049 (5.9%)	--	--
hemicellulase	0.029 (3.4%)	--	--
PES	0.226 (27.0%)	--	--
total identified	**0.424 (50.6%)**	**0.007 (0.8%)**	**0.417 (49.8%)**

nd not detected

1 material which eluted in or near void volume; isolated and subjected to hydrolysis with mild acid, mild base, and strong acid (cotton gin byproduct only), resulting chromatograms were not significantly different from the unhydrolyzed sample

2 radioactivity which eluted after void volume and prior to any available bifenazate or bifenazate metabolites

3 hexane extract was saponified and the resulting extract partitioned with hexane; the hexane partition was HPLC analyzed and resulted in peaks with nearly identical retention times to linoleic acid, palmitic acid, and oleic acid (quantitative data was not provided)

4 sequentially hydrolyzed with protease, 72% sulfuric acid, and 1N NaOH

5 confirmed by MS analysis

6 confirmed by TLC analysis

7 radioactivity was isolated and subjected to hydrolysis with mild acid, mild base, strong acid, and β-glucosidase; resulting chromatograms were not significantly different from the unhydrolyzed sample except for the strong acid hydrolysate from the 26-29 minute region which resulted in the identification of A1530 and D9963

Cotton Metabolism Summary: TRR in cottonseed harvested 112 DAT with [^{14}C]bifenazate (substituted phenyl ring labeled) at 2.0 lbs ai/acre (2.7x the maximum proposed seasonal rate) were 0.125 ppm. The cottonseed was homogenized with hexane (23% TRR) and ACN:water (50:50; 14% TRR). Bifenazate, D3598, D4642, and D1989 were identified in the extracts at concentrations <0.1% TRR. The majority of the radioactivity in the hexane extract eluted as a single peak with a retention time indicative of a non-polar compound. The hexane extract was saponified, partitioned with hexane (21% TRR), and the hexane partition HPLC analyzed. The resulting chromatogram yielded peaks with nearly identical retention times to linoleic acid, palmitic acid, and oleic acid (quantitative data was not provided). Protease and strong acid hydrolysis of the PES (63% TRR) released 25% and 12% of the TRR, respectively.

TRR in cotton gin byproduct harvested 112 DAT with [^{14}C]bifenazate (substituted phenyl ring labeled) at 2.0 lbs ai/acre (2.7x the maximum proposed seasonal rate) were 0.838 ppm. The cotton gin byproduct was homogenized with ACN (56% TRR) and ACN:water (50:50; 26% TRR). Bifenazate was identified in the extracts at 40% of the TRR. D3598, D1989, D4642, A1530 (hydrolysis product), and D9963 (hydrolysis product) were also identified but at concentrations ≤6% of the TRR. Cellulase and hemicellulase hydrolysis of the PES (34% TRR) released 6% and 3% of the TRR, respectively.

The petitioner proposed metabolic pathway indicates that bifenazate is initially oxidized to D3598 which is further degraded to D1989, D4642, A1530, and D9963. The data indicate that some of the radioactivity was incorporated into fatty acids of triglyceride and either conjugated or incorporated into protein and carbohydrates (see attachment 4).

Conclusion; Nature of the Residue - Plant: The MARC reviewed the apple, orange, and cotton metabolism studies and determined that for tolerance expression and risk assessment purposes, the residues of concern in these crops are bifenazate and D3598 (expressed as bifenazate). The metabolic route in apple, orange, and cotton were similar and proceeded via oxidation of the hydrazine moiety of bifenazate to form D3598 which is further degraded to D1989, D9963, D4642, and/or A1530 and to bound residues by reaction with natural products. Since only fruit and oilseed metabolism studies have been submitted, the nature of the residue in all plants is not understood. A metabolism study conducted on a third dissimilar crop (i.e. root/tuber vegetable (root/tuber vegetable in which the leaves are monitored), small grain, Brassica vegetable, or leafy vegetable) is needed prior to drawing conclusions concerning the nature of the residue in all plants (biphenyl hydrazine should be monitored; D276801, T. Bloem, 16-Aug-2001). For the purposes of this petition, HED concludes that the nature of the residue in apple, orange, and cotton are appropriate for translation to pome fruit, nectarine, peach, plum, grape, strawberry, cotton, and hops.

OPPTS GLN 860.1300: Nature of the Residue - Livestock

MRID 45052301: Metabolism of [^{14}C]D2341 in Lactating Goats: The in-life and analytical portions of the study were performed by Ricerca, Inc. (Painesville, OH). After the morning milking for 4 consecutive days, a goat was orally administered [^{14}C]bifenazate (21.5 mg/day; substituted phenyl ring labeled; specific activity ~40,780 dpm/µg). The animal was feed Purina Rumilab Chow® and water *ad libitum*. Based on wet feed weight, the dose and feed consumption yielded a dietary burden of 10 ppm (1.7x MTDB).

Milk samples were collected twice daily (a.m. and p.m.) and combined. Urine and feces were collected daily. The animal was sacrificed on the 4th day approximately 9 hours after the last dose. The following samples were collected: blood, kidneys, liver, loin muscle, rear leg muscle, omental fat, and perirenal fat. All samples were homogenized and analyzed for TRR. A total of 20% and 46% of the administered dose was excreted in the urine and feces, respectively (68% of the administered dose was recovered). Table 7 is a summary of the TRR in milk and tissue.

Table 7: TRR in Lactating Goat

	ppm[1]	% TAD[2]
milk day 1	0.025	total = 0.22
day 2	0.029	
day 3	0.032	
day 4	0.047	
blood	0.120	0.28
omental fat	0.104	0.03
perirenal fat	0.125	0.01
kidneys	0.263	0.04
liver	1.773	1.60
rear leg muscle	0.014	0.01
loin muscle	0.013	0.01

[1] ppm bifenazate equivalents
[2] % of the total administered dose

Extraction and Characterization of Residues: Samples of liver, kidney, muscle, milk, and fat were subjected to extraction and hydrolysis procedures for residue identification/characterization. The following paragraphs summarizes these procedures. Table 4 summarizes the radioactive distribution and metabolite identification.

Milk (collected on day 4; 0.047 ppm): Milk was mixed with ethyl acetate and centrifuged. The supernatant (94% TRR) was collected, reduced to the aqueous phase, and partitioned with hexane (hexane - 11% TRR; aqueous - 84% TRR). The PES (4% TRR) were not further analyzed.

Rear Leg and Loin Muscle (0.014 and 0.013 ppm, respectively): The rear leg and loin muscle samples were homogenized with ACN (rear leg - 58% TRR; loin - 61% TRR) and ACN:water (1:1; rear leg and loin - <LOD (<0.007 ppm)). The PES (rear leg -33% TRR; loin - 40% TRR) were not further analyzed.

Omental and Perirenal Fat (0.104 and 0.125 ppm, respectively): The omental and perirenal fat samples were homogenized with ACN (omental - 86% TRR; perirenal - 76% TRR) and ACN:water (1:1; omental and perirenal - <LOD (<0.007 ppmn)). The PES of omental (21% TRR) and perirenal (10% TRR) fat were saponified with isopropyl alcohol and 1N NaOH. The resulting solution was acidified to pH 1 and partitioned with hexane (omental - 6% TRR; perirenal - 4% TRR) and ethyl acetate (omental - 5% TRR; perirenal - 4% TRR). A total of 3% TRR (omental) and 2% TRR (perirenal) remained in the aqueous phase.

Kidney (0.263 ppm): The kidney sample was homogenized with ACN (39% TRR) and ACN:water (1:1; 10% TRR). The PES (47% TRR) were treated with 5% SDS and 25mM dithiothreitol solution (50 C 16 hours). The samples were centrifuged and the supernatant was collected (42% TRR) and analyzed by gel permeation chromatography (GPC). Based on the GPC analysis, the kidney SDS hydrolysate consisted of a region of high molecular weight and a region of low molecular weight. The high molecular weight fractions were pooled and the protein content was determined to be 28% of the TRR.

A sample of unextracted kidney homogenate was treated with non-specific protease enzymes (37 C, 6 days). The resulting mixture was lyophilized and extracted with methanol (75% TRR; 12% TRR remained as unextracted material). The methanol extract was concentrated, loaded onto a C18 column, and fractionated by eluting the C18 column with water and then water mixed with increasing %ACN until the eluent was 100% ACN. The majority of the radioactivity eluted in the 25%, 50%, and 75% ACN fractions (22%, 27%, and 8% TRR, respectively; the remaining fractions contained ≤3% TRR (≤0.009 ppm)). The major C18 column fractions were partitioned with methylene chloride at acidic and neutral pH (for the 25% and 75 % ACN eluents the majority of the radioactivity remained in the aqueous phase; for the 50% ACN eluent the majority of the radioactivity was found in the methylene chloride phase). The 25%, 50%, and 75% ACN fractions were also HPLC analyzed. No radioactivity in the resulting chromatograms could be associated with available standards although the chromatograms were qualitatively similar to the 25%, 50%, and 75% ACN fractions of the liver non-specific protease hydrolysate (see below).

A second sample of unextracted kidney homogenate was treated with trypsin (37 C, 24 hours) followed by pepsin (37 C, 2 days). The resulting mixture was centrifuged and the supernatant collected (32% TRR). The remaining solids (38% TRR) were dried and extracted with methanol (45% TRR; 7% TRR remained as unextracted material). The trypsin/pepsin hydrolysate and the methanol extract were combined (65% TRR), concentrated, loaded onto a C18 column, and fractionated by eluting the C18 column with water and then water mixed with increasing %ACN until the eluent was 100% ACN. The majority of the radioactivity eluted in the 25%, 50%, and 75% ACN fractions (28%, 18%, and 8% TRR, respectively; the remaining fractions contained ≤4% TRR). The major C18 column fractions were partitioned with methylene chloride at acidic and neutral pH (majority of the radioactivity remained in

the aqueous phase). The 25%, 50%, and 75% ACN fractions were also HPLC analyzed. No radioactivity in the resulting chromatograms could be associated with available standards although the chromatograms were qualitatively similar to the 25%, 50%, and 75% ACN fractions of the liver trypsin/pepsin hydrolysate (see below).

Liver (1.773 ppm): The liver sample was homogenized with ACN (7% TRR) and ACN:water (1:1; 3% TRR). The PES (87% TRR) were treated with 5% SDS and 25mM dithiothreitol solution (50 C 16 hours). The samples were centrifuged and the supernatnant was collected (78% TRR) and analyzed by gel permeation chromatography (GPC). Based on the GPC analysis, the liver SDS hydrolysate consisted of a regions of high molecular weight compounds (75% TRR) and a region of low molecular weight compounds (3% TRR). The high molecular weight fractions were pooled and the protein content was determined to be 50% of the TRR. A sub-sample of the SDS hydrolysate was subjected to ultrfiltration with a membrane having a molecular weight cut off of 10,000. Approximately, 75% of the TRR was retained by the filter.

A sub-sample of liver homogenate was refluxed with 6N HCl (18 hours, 100 C). The collected hydroslyate (3% TRR) was partitioned with methylene chloride (1% TRR). The remaining aqueous phase was partitioned with ethyl acetate at acidic (1% TRR) and neutral (<1% TRR) pH (2% TRR remained in the aqueous phase). The methylene chloride and acidic ethyl acetate partitions were HPLC analyzed (no radioactivity could be associated with available standards).

A sub-sample of liver homogenate was refluxed with 10N NaOH (18 hours, 100 C). The collected hydroslyate (97% TRR) was partitioned with hexane which was subsequently partitioned with ACN (ACN - 8% TRR; hexane - 12% TRR). The aqueous phase remaining after partitioning with hexane was partitioned with ethyl acetate (ethyl acetate - 29% TRR; aqueous - 24% TRR). The ACN and ethyl acetate partitions were HPLC analyzed (no radioactivity could be associated with available standards). The petitioner indicated that no additional work was carried out on the solubilized material due the harsh hydrolytic conditions used to release the residues.

A sample of unextracted liver homogenate was treated with non-specific protease enzymes (37 C, 6 days). The resulting mixture was lyophilized and extracted with methanol (61% TRR; 22% TRR remained as unextracted material). The methanol extract was concentrated, loaded onto a C18 column, and fractionated by eluting the C18 column with water and then water mixed with increasing %ACN until the eluent was 100% ACN. The majority of the radioactivity eluted in the 25%, 50%, and 75% ACN fractions (8%, 36%, and 4% TRR, respectively; the remaining fractions contained ≤5% TRR). The major C18 column fractions were partitioned with methylene chloride at acidic and neutral pH (majority of the radioactivity remained in the aqueous phase). The 25%, 50%, and 75% ACN fractions were also HPLC analyzed (D9569 and A1530 were identified).

A sample of unextracted liver homogenate was treated with trypsin (37 C, 24 hours) followed by pepsin (37 C, 2 days). The resulting mixture was centrifuged and the supernatant collected (13% TRR). The remaining solids (70% TRR) were dried and extracted with methanol (40% TRR; 22% TRR remained as unextracted material). The trypsin/pepsin hydrolysate and the methanol extract were concentrated, loaded onto separate C18 columns, and fractionated by eluting the C18 column with water and then water mixed with increasing %ACN until the eluent was 100% ACN. For the hydrolysate, the majority of the radioactivity eluted in the 25% and 50% ACN fractions (7% and 2% TRR, respectively; remaining fractions were ≤0.1% TRR (≤0.002 ppm)). For the methanol extract, the majority of the radioactivity eluted in the 25%, 50%, and 75% ACN fractions (8%, 11%, and 3% TRR, respectively; the remaining fractions contained ≤8% TRR). The major fractions were partitioned with methylene chloride at acidic and neutral pH (majority of the radioactivity remained in the aqueous phase). The 25% and 50% ACN fractions were also HPLC analyzed (no radioactivity in the resulting chromatograms could be associated with available standards).

Instrumental Analysis: The hexane and aqueous extracts of milk, the ACN and ACN:water extracts of tissues, and the major fractions from the protease and trypsin/pepsin hydrolysis of liver and kidney were HPLC analyzed. Residues were identified by cochromatography with the following standards: bifenazate, D3598, D8654, A1530, D1989, D9569, D9477, D9474, bifenazate-glucuronide (isolated from rat metabolism study), and A1530-sulfate (isolated from rat metabolism study). The HPLC effluent was monitored by an in-line radioactivity flow detector and quantitation was by fraction collection followed by LSC analysis (LOQ = 0.0001 ppm).

A radioactive peak which did not correspond with the available standards was identified in the liver, kidney, muscle, and fat extracts (retention time of ~16 minutes). A similar peak was identified and isolated in the rat metabolism study and using a different HPLC system the peak was resolved into several separate peaks including peaks corresponding to bifenazate-glucuronide (identified via NMR analysis) and A1530-glucuronide (identified via isolation and hydrolysis with glucuronidase/sulfatase followed by HPLC analysis). The unknown radioactive peak from the liver ACN extract was isolated and analyzed using the HPLC system developed in the rat metabolism study. Bifenazate-glucuronide was identified via coinjection with bifenazate-glucuronide isolated from the rat metabolism study and A1530-glucuronide was identified by isolation and hydrolysis with glucuronidase/sulfatase followed by HPLC analysis. This unknown radioactive peak from the kidney ACN extract was isolated and analyzed using the HPLC system developed in the rat metabolism study. Based on retention time, A1530-glucuronide and A1530-sulfate were identified.

The non-specific protease digestion of liver homogenate released a major portion of the liver bound residues (61% TRR), the majority of which was present in the 50% ACN C18 column fraction (36% TRR). Since this fraction contained a significant portion of TRR, the petitioner performed several procedures to better characterize/identify the residues including hydrolysis (glucuronidase/sulfatase), GPC analysis, cation/anion exchange chromatography, HPLC analysis, and LC/MS/MS analysis. Based on these experiments, it was concluded that the protease released radioactivity consisted of partially digested peptides of intermediate weight. LC/MS/MS analysis resulted in the identification of 2 compounds with molecular ions of 464 and 363. Based on the mass spectral data and the results from the other experiments the petitioner proposed that these two compounds were threonyl-tyrosine (0.079 ppm, 4% TRR) and tyrosine (0.116, 7% TRR) adducts of oxidized D9569 (see attachment 1 for structures).

Storage Stability: All samples were frozen after collection and remained frozen until analysis. HPLC chromatograms from the initial analysis of the extractable residues in milk and tissues were compared to the chromatograms attained after 80-216 days of frozen storage (15 days for fat). The qualitative appearance of the initial and final chromatograms were similar for milk, fat, and liver. Some qualitative changes were observed in muscle and kidney extracts. The petitioner indicated that the initial and analysis of milk and tissue samples was conducted within 5 weeks of collection. Since the initial analysis occurred within ~30 days of harvest, the submitted storage stability data are sufficient to validate this study.

Table 8: Identification/Characterization of TRR in Goat Tissue and Milk

	ppm bifenazate equivalents (%TRR)						
	liver	kidney	muscle		fat		day 4 milk
			loin	leg	omental	perirenal	
total	1.773	0.263	0.013	0.014	0.104	0.125	0.047
extractable[1]	0.175 (9.86%)	0.129 (49.15%)	0.008 (61.29%)	0.008 (58.54%)	0.090 (86.26%)	0.096 (76.45%)	0.044 (94.78%)
bifenazate	0.011 (0.62%)	0.003 (1.30%)	0.001 (4.25%)	nd	0.061 (58.54%)	0.066 (53.13%)	<0.001 (0.54%)
D3598	0.006 (0.36%)	0.005 (1.87%)[2]	0.001 (4.46%)	<0.0005 (2.72%)	0.009 (8.77%)	0.006 (4.88%)	0.004 (8.16%)
D1989	0.006 (0.35%)		0.001 (4.00%)	0.001 (3.78%)	0.003 (2.67%)	0.004 (2.85%)	0.002 (3.58%)
A1530	0.100 (5.61%)[3]	0.036 (13.52%)[3]	0.002 (13.64%)	0.002 (11.55%)	0.006 (6.19%)	0.007 (5.50%)	0.001 (1.61%)
D9569	0.029 (1.64%)[3]	0.005 (1.32%)[3]	nd	nd	nd	nd	nd
A1530-sulfate	0.005 (0.28%)	0.029 (11.12%)	nd	nd	nd	nd	0.019 (40.70%)
A1530-glucuronide	0.017 (0.93%)	0.004 (1.60%)	nd	nd	nd	nd	nd
bifenazate-glucuronide	0.005 (0.29%)	nd	nd	nd	nd	nd	nd
conjugates	nd	nd	0.002 (18.58%)[4]	0.003 (21.92%)[4]	0.004 (3.98%)[4]	0.005 (3.60%)[4]	nd
unknowns[5]	0.113 (6.38%)	0.074 (28.13%)	0.002 (16.36%)	0.003 (18.56%)	0.007 (6.11%)	0.008 (6.48%)	0.022 (46.77%)
PES	1.543 (87.01%)	0.123 (46.89%)	0.005 (39.63%)[6]	0.005 (33.47%)[6]	0.021 (20.60%)[6]	0.013 (10.46%)[6]	0.002 (3.86%)[6]
total identified	**0.179 (10.10%)**	**0.081 (30.73%)**	**0.003 (26.35%)**	**0.003 (18.05%)**	**0.079 (76.17%)**	**0.083 (66.36%)**	**0.026 (54.59%)**
hydrolysis experiments with liver and kidney homogenate[7]			--	--	--	--	--
6N HCl	0.059 (3.35%)	--	--	--	--	--	--
10N NaOH	1.713 (96.63%)	--	--	--	--	--	--
protease	1.513 (85.33%)[8]	0.198 (75.21%)	--	--	--	--	--
trypsin/pepsin	0.236 (13.32%)	0.172 (65.36%)	--	--	--	--	--

nd not detected

1 ACN and ACN:water in 1% ethyl acetate (1:1) extractable residues for tissues; hexane and aqueous extractable residues for milk

2 D1989 and D3598 coelluted in kidney

3 includes A1530 and D9569 identified in the protease hydrolysate

4 by analogy to a peak isolated and further characterized in liver and kidney may contain A1530-sulfate, A1530-glucuronide, bifenazate-glucuronide, and other compounds

5 unidentified peaks and diffuse radioactivity (liver - ≤0.033 ppm, ≤1.86% TRR; kidney - ≤0.023 ppm, ≤8.89% TRR; loin muscle - ≤0.001 ppm, ≤11.25%; leg muscle - ≤0.002 ppm, ≤13.76%; omental fat - ≤0.006 ppm, ≤5.33%; perirenal fat - ≤0.006 ppm, ≤5.33%; milk - ≤0.007 ppm, ≤15.00%)

6 refer to text for characterization procedures performed on these matrices

7 sub-samples of unextracted liver and kidney homogenate were hydrolyzed for characterization of unextracted residues

8 LC/MS/MS analysis of a portion of the released radioactivity resulted in the identification of 2 compounds with molecular ions of 464 and 363; based on the mass spectral data and the results from the other experiments the petitioner proposed that these two compounds were threonyl-tyrosine (0.079 ppm, 4% TRR) and tyrosine (0.116 ppm, 7% TRR) adducts of oxidized D9569 (see attachment 1 for structures); the remainder of the protease released radioactivity was characterized as partially digested peptides of intermediate weight

Lactating Goat Metabolism Summary: A lactating goat was orally administered [^{14}C]bifenazate for 4 consecutive days (substituted phenyl ring labeled; dietary burden of 10 ppm based on wet feed weight; 1.8x the MTDB). The animal was sacrificed on the fourth day approximately 9 hours after the last dose and the following samples were collected: blood (0.120 ppm), kidneys (0.263 ppm), liver (1.773 ppm), loin muscle (0.013 ppm), rear leg muscle (0.014 ppm), omental fat (0.104 ppm), and perirenal fat (0.125 ppm). Milk samples were collected twice daily (a.m. and p.m. samples were combined) and reached a maximum residue on day 4 of 0.047 ppm. Radioactive analysis of the urine and feces indicated that 20% and 46% of the administered dose was excreted, respectively (total recovery of administered dose was 68%).

The majority of the residues in milk (hexane and water; 95% TRR), fat (ACN and ACN:water; 76% - 86% TRR), and muscle (ACN and ACN:water; 59% - 61% TRR) were extractable. The major residue identified in these extracts were as follows: milk (A1530-sulfate - 41% TRR), fat (bifenazate - 53% - 59% TRR), and muscle (A1530 - 12% - 14% TRR). D3598 and D1989 were also detected in milk, fat, and muscle (≤9% TRR). The PES of milk (4% TRR) and muscle (33 - 40% TRR) were not further analyzed while the PES of fat (10 - 21% TRR) were saponified. The resulting solution was partitioned with hexane (4-6% TRR) and ethyl acetate (4-5% TRR; 2-3% TRR remained in the aqueous phase).

Approximately 10% of the TRR in liver was ACN and ACN:water extractable. HPLC analysis of the extractable residue resulted in the detection of bifenazate, D3598, D1989, A1530, A1530-glucuronide, A1530-sulfate, and bifenazate-glucuronide (≤1% TRR). The liver PES occupied 87% of the TRR. Procedures conducted with non-specific protease, trypsin/pepsin, SDS and 25 mM dithiothreitol solubilization, GPC analysis, and measurement of protein content suggested that the unextracted radioactivity was covalently bound to liver protein. Analysis of the non-specific protein hydrolysate of unextracted liver homogenate resulted in the identification of A1530 (6% TRR) and D9569 (2% TRR) and preliminary identification of threonyl-tyrosine (0.079 ppm, 4% TRR) and tyrosine (0.116, 7% TRR) adducts of oxidized D9569 (see attachment 1 for structures).

Approximately 49% of the TRR in kidney was ACN and ACN:water extractable. The major residue identified in these extracts was A1530-sulfate (11% TRR). Minor amounts of bifenazate, D3598, A1530, and A1530-glucuronide were also detected (<3% TRR). The kidney PES occupied 47% TRR. Procedures conducted with non-specific protease, trypsin/pepsin, SDS solubilization, GPC analysis, and measurement of protein content suggested that the unextracted radioactivity was covalently bound to kidney protein. Analysis of the non-specific protein hydrolysate of unextracted kidney homogenate resulted in the identification of A1530 (14% TRR) and D9569 (1% TRR).

The petitioner's proposed metabolic pathway includes several metabolic reactions including hydrazine oxidation, demethylation, loss of the hydrazinecarboxylic acid portion of the molecule, hydroxylation, conjugation with glucuronic acid or sulfate, and covalent binding with amino acids of proteins (see attachment 5).

MRID 45052225: Metabolism of [^{14}C]D2341 in Laying Hens: The in-life and analytical portions of the study were performed by Ricerca, Inc. (Painesville, OH). For 4 consecutive days, 10 laying hens were orally administered [^{14}C]bifenazate (~1.4 mg/day; substituted phenyl ring labeled; specific activity ~40,000 dpm/µg). The birds were fed Purina Layena No. 6501 and water *ad libitum*. Based on wet feed weight, the dose and feed consumption yielded a dietary burden of 11 ppm (110x MTDB).

Eggs were collected twice daily and separated into yolk and white. Eggs collected in the afternoon were refrigerated until the following day and then combined with the morning collection. Excreta was collected daily. The animals were sacrificed on the 4th day approximately 9 hours after the last dose. The following samples were collected: blood, liver, thigh muscle, breast muscle, and skin with fat. All

samples were pooled by type, homogenized, and analyzed for TRR. A total of 81% of the administered dose was excreted (85% of the administered dose was recovered). Table 9 is a summary of the TRR in egg and tissue.

Table 9: TRR in Laying Hens

	ppm bifenazate equivalents	%TAD
egg white (day 1)	<0.003	0.01
egg white (day 2)	<0.003	
egg white (day 3)	<0.003	
egg white (day 4)	<0.003	
egg yolk (day 1)	<0.003	
egg yolk (day 2)	0.004	
egg yolk (day 3)	0.014	
egg yolk (day 4)	0.025	
liver	0.613	0.51
skin with fat	0.048	0.02
breast muscle	<0.005	--
thigh muscle	0.006	0.01
blood	0.210	0.85

Extraction and Characterization of Residues: Samples of liver, thigh muscle, skin with fat, and egg yolk were subjected to extraction and hydrolysis procedures for residue identification/characterization. The following paragraphs summarize these procedures. Since the TRR in breast muscle and egg white were below the limit of detection, no extraction or chromatographic analysis were performed on these matrices. Table 10 summarizes the radioactive distribution and metabolite identification.

Egg Yolk (day 4 - 0.025 ppm): The day 4 egg yolk sample was homogenized with ACN and the resulting extract was partitioned with hexane (hexane - 2% TRR; ACN - 48% TRR). The remaining solids were extracted with ACN:water (1:1 with 1% ethyl acetate; 23% TRR). PES were 26% of the TRR.

A sub-sample of day 4 egg yolk was extracted according to the Bligh-Dyer extraction procedure to determine the nature of the nonpolar extractable residues from egg yolks. The egg yolk was homogenized with methylene chloride (55% TRR) and methanol/water (18% TRR). The methylene chloride extract was concentrated and partitioned with ACN (28% TRR) and hexane (38% TRR). Unextractable residues were 36% of the TRR.

Skin with Fat (0.048 ppm): The skin with fat sample was homogenized with ACN and the resulting extract was partitioned with hexane (hexane - 3% TRR; ACN - 51% TRR). The remaining solids were extracted with ACN:water (1:1 with 1% ethyl acetate; 5% TRR). PES were 31% of the TRR.

The PES from the storage stability sample (25% TRR) were saponified with isoprpopyl alcohol and 1N NaOH (3 hours). The solution was cooled, acidified, and sequentially partitioned with hexane (5% TRR) and ethyl acetate (11% TRR; 7% TRR remained in the aqueous phase).

Thigh Muscle (0.006 ppm): The muscle sample was homogenized with ACN (41% TRR) followed by ACN:water (1:1 with 1% ethyl acetate; 20% TRR). PES were 46% of the TRR.

Liver (0.613 ppm): The liver sample was homogenized with ACN and the resulting extract was partitioned with hexane (hexane - 1% TRR; ACN - 8% TRR). The remaining solids were extracted with ACN:water (1:1 with 1% ethyl acetate; 20% TRR). The PES (61% TRR) were treated with an aqueous solution containing 5% SDS and 25mM dithiothreitol (50 C overnight). This treatment quantitatively solubilized the unextracted residue and the resulting hydrolysate was GPC analyzed. Based on GPC analysis, the majority of the solubilized radioactivity consisted of high molecular weight material (46% TRR) with a small amount of low molecular weight material. The high molecular weight material was pooled and the protein content was 42% TRR.

A sample of unextracted liver homogenate was hydrolyzed with a non-specific protease (37 C, 6 days). The resulting supernatant was collected (46% TRR), loaded on a C18 column, and fractionated by eluting the C18 column with water and then water mixed with increasing %ACN until the eluent was 100% ACN. The majority of the radioactivity eluted in the 100% H_2O (2% TRR) and 25% ACN fractions (37% TRR; the remaining fractions contained ≤1% TRR). HPLC analysis of the 100% H_2O fraction resulted in three components which eluted near the void volume (<0.01 ppm; no further analytical work was performed). HPLC analysis of 25% ACN fraction resulted in the identification of 2 major components each >0.05 ppm. To further characterize the 25% ACN fraction, the following procedures were conducted: **(1)** Aliquots were treated with glucuronidase/sulfatase and 1% acetic acid (hydrolyzes N-glucuronides). The resulting hydrolysates were HPLC analyzed and no change in the HPLC profile was observed; **(2)** Ultrafiltration of an aliquot of the 25% ACN fraction was conducted. Radioactivity in the sample quantitatively passed through a 10,000 and 3,000 molecular weight cut-off filters. A 1,000 molecular weight cut-off filter retained 44% of the radioactivity in the fraction (16% TRR) while 42% passed through (15% TRR); and **(3)** An aliquot of the 25% ACN fraction was derivatized with potassium carbonate/methyl iodide to determined if phenyl hydroxyl and/or carboxylic acid moieties were present. The resulting derivatized sample was HPLC analyzed and the profile was significantly different from the underivatized sample.

The solids remaining after protease extraction of the unextracted liver homogenate were extracted with methanol (32% TRR; 21% TRR remained unextracted). The methanol extract was reduced to the aqueous phase and partitioned with methylene chloride (aqueous - 15% TRR; methylene chloride - 18% TRR). An excess of ACN was added to the methylene chloride phase and the mixture was concentrated until only ACN and solids remained. The ACN phase was collected (10% TRR) and the solids were extracted with methanol (methanol- 5% TRR; solids - 1% TRR). The aqueous, ACN, and methanol phases were HPLC analyzed (A1530 was identified in the ACN phase).

Instrumental Analysis: The ACN extract of thigh muscle; the ACN phases of day 4 egg yolk, skin with fat, and liver; the ACN:water extract of liver; and the major fractions resulting from protease hydrolysis of liver were HPLC analyzed. Residues were identified by cochromatography with the following standards: bifenazate, D3598, D8654, A1530, D1989, D9569, D9477, D9474, bifenazate-glucuronide (isolated from rat metabolism study), and A1530-sulfate (isolated from rat metabolism study). The HPLC effluent was monitored by an in-line radioactivity flow detector and quantitation was by fraction collection followed by LSC analysis (LOQ = 0.0001 ppm).

Storage Stability: All samples were frozen after collection and remained frozen until analysis. HPLC chromatograms from the initial analysis of the extractable residues in milk and tissues were compared to the chromatograms attained after 121-171 days of frozen storage. The qualitative appearance of the initial and final chromatograms were similar for egg yolk, skin with fat, and liver. Some qualitative changes were observed in the ACN extract of thigh muscle. The petitioner indicated that the initial analysis of egg yolk and tissue samples was conducted within ~100 days of collection. Since TRR in thigh muscle were <0.01 ppm and therefore did not require additional identification/characterization, the submitted storage stability data are sufficient to validate this study.

Table 10: Identification/Characterization of TRR in Laying Hens

	ppm bifenazate equivalents (%TRR)			
	liver	skin with fat	thigh muscle	day 4 egg yolk
total	0.613	0.048	0.006	0.025
extractable[1]	0.185 (30.10%)	0.028 (58.46%)	0.004 (61.18%)	0.018 (70.24%)
bifenazate	0.002 (0.28%)	0.001 (2.85%)	nd	0.005 (18.47%)
D3598	0.002 (0.37%)	0.008 (15.71%)	<0.0005 (2.75%)	0.001 (3.29%)
D1989	0.001 (0.18%)	0.005 (10.36%)	nd	0.001 (5.09%)
A1530	0.038 (6.20%)[2]	0.001 (2.67%)	<0.0005 (1.61%)	0.001 (4.91%)
conjugates[3]	0.017 (2.81%)	0.001 (1.97%)	<0.0005 (3.65%)	<0.0005 (1.75%)
unknowns[4]	0.148 (23.77%)	0.012 (25.17%)	0.003 (53.17%)	0.010 (39.33%)
total identified	0.035 (5.78%)	0.016 (33.57%)	<0.0005 (8.01%)	0.008 (33.51%)
PES	0.372 (60.67%)	0.012 (24.66%)	0.003 (46.36%)	0.007 (26.17%)
saponification	np	0.012 (24.66%)	np	np
hexane	np	0.002 (5.12%)	np	np
ethyl acetate	np	0.005 (11.09%)	np	np
aqueous	np	0.004 (7.49%)	np	np
5% SDS	0.372 (60.67%)[5]	np	np	np
hydrolysis exp. with liver homogenate[6]		np	np	np
protease	0.284 (46.40%)[7]	np	np	np

np not performed
nd not detected
1 ACN and ACN:water in 1% ethyl acetate (1:1) extractable residues
2 includes A1530 identified in the protease hydrolysate
3 may contain bifenazate-glucuronide; peak with the same retention time which was isolated from excreta and found to contain bifenazate-glucuronide
4 unidentified peaks and diffuse radioactivity (egg yolk - ≤0.006 ppm, ≤23.21% TRR; skin with fat - ≤0.008 ppm, ≤15.86% TRR; thigh muscle - ≤0.001 ppm, ≤19.86%; liver - ≤0.046 ppm, ≤7.51%)
5 GPC analysis followed by a protein assay indicated that 41% TRR was associated high molecular weight proteins
6 sub-samples of unextracted liver homogenate were hydrolyzed for characterization of unextracted residues
7 ultrafiltration and derivatization with potassium carbonate/methyl iodide indicated that the solubilized radioativity was associated with phenolic and/or carboxylic acid moieties with molecular weight distribution of <1,000 to 3,000

Laying Hen Metabolism Summary: Ten laying hens were orally administered [^{14}C]bifenazate for 4 consecutive days (substituted phenyl ring labeled; dietary burden of 11 ppm based on wet feed weight). The animals were sacrificed on the fourth day approximately 9 hours after the last dose and the following samples were collected: blood (0.210 ppm), skin with fat (0.048 ppm), liver (0.613 ppm), breast muscle (<0.005 ppm), and thigh muscle (0.006 ppm). Egg samples were collected twice daily (a.m. and p.m.; eggs collected in the p.m. were combined with the following a.m. samples). Residues in egg white were <0.003 ppm while residues in egg yolk reached a maximum residue on day 4 of 0.025 ppm. Radioactive analysis of excreta indicated that 81% of the administered dose was excreted (total recovery of administered dose was 85%). Since the TRR in breast muscle and egg white were <0.005 ppm, no extraction or chromatographic analysis were performed on these matrices.

The majority of the residues in skin with fat (58% TRR), thigh muscle (61% TRR), and day 4 egg yolk (70% TRR) were ACN and ACN:water extractable. The major residues identified in skin with fat were D3598 (16% TRR) and D1989 (10% TRR; bifenazate and A1530 were also identified but at <3% TRR). The major residue in day 4 egg yolk was bifenazate (18% TRR; D3598, D1989, and A1530 were also identified but at ≤5% TRR). No residue was identified in thigh muscle at a concentration >10% TRR (D3598 and A1530 were identified at a concentration <3% TRR).

Approximately 30% of the TRR in liver was ACN and ACN:water extractable. HPLC analysis of the extractable residue resulted in the detection of bifenazate, D3598, D1989, and A1530 (≤1% TRR). Levels of unextracted radioactivity in liver were 61% TRR. The unextracted radioactivity was completely solubilized upon hydrolysis with 5% SDS and 25 mM dithiothreitol. GPC analysis followed by a protein assay of the SDS hydrolysate indicated that 41% TRR was associated with high molecular weight proteins.

A sample of unextracted liver homogenate was hydrolyzed with a non-specific protein (hydroslyate - 46% TRR; A1530 was identified in the resulting hydroslyate). Ultrafiltration and derivatization with potassium carbonate/methyl iodide indicated that the solubilized radioativity was associated with phenolic and/or carboxylic acid moieties with molecular weight distribution of <1,000 to 3,000

The petitioner's proposed metabolic pathway includes several metabolic reactions including hydrazine oxidation, demethylation, loss of the hydrazinecarboxylic acid portion of the molecule, hydroxylation, conjugation with glucuronic acid, and covalent binding with amino acids of proteins (see attachment 6).

Conclusion; Nature of the Residue - Livestock: The MARC reviewed the goat and hen metabolism studies and determined that for tolerance expression and risk assessment purposes, the residues of concern in livestock tissue (excluding fat), eggs, and milk are bifenazate, D3598 (expressed as bifenazate), A1530, and A1530-sulfate (expressed as A1530). The residues of concern for tolerance expression and risk assessment purposes in fat are bifenazate and D3598 (expressed as bifenazate). The metabolic route in goats and hens were similar and proceeded via oxidation of the hydrazine moiety of bifenazate to form D3598, loss of the hydrazinecarboxylic acid portion of the molecule, followed by demethylation, hydroxylation, conjugation with glucuronic acid or sulfate, and covalent binding with amino acids of proteins (D276801, T. Bloem, 16-Aug-2001).

OPPTS GLN 860.1340: Residue Analytical Method

Plants: The petitioner is proposing method UCC-D2341 for enforcement of the proposed plant tolerances. The method was developed by Ricerca, Inc. (Painesville, OH). The petitioner indicated that the LOQ and the limit of detection (LOD) for all analytes in the analyzed matrices were 0.01 ppm and 0.005 ppm, respectively. A summary of the proposed enforcement method follows.

Method UCC-D2341: The crop sample is homogenized with 100 ml of ACN with 0.1% acetic acid (2x). The extracts are combined, filtered, and brought to 250 ml volume with ACN. A 50 ml aliquot of the extract is partitioned with methylene chloride. The methylene chloride phase is collected, evaporated to dryness, and the residue reconstituted with the HPLC mobile phase containing 0.05% ascorbic acid (the ascorbic acid reduces D3598 to bifenazate). After incubation for 2-6 hours, the samples are quantified via HPLC with an oxidative coulometric electrochemical detector.

The petitioner submitted radiovalidtion data in support of the proposed enforcement method (MRID 45052316; conducted by Ricerca, Inc; 20-Aug-1998). Apple and orange samples from the previously summarized metabolism studies were analyzed for bifenazate and D3598 using the proposed enforcement method and using a HPLC-RAD method. Table 11 summarizes the radiovalidation results.

As stated earlier, the proposed plant enforcement method was developed by Ricerca, Inc. (Painesville, OH). In support of the independent laboratory validation (ILV) requirement, the petitioner submitted MRID 45052311 (performed by the petitioner - Uniroyal Chemical Company, Inc. (Middlebury, CT)). The petitioner also submitted 4 studies which provide validation data for the proposed enforcement method in/on several crops (MRIDs 45052314, 45052315, 45052316 and 45052317; all of the studies were conducted by Ricerca, Inc. (Painesville, OH); August 1998 - August 1999). The analytical methods used in the field trial and processing studies were the same as the proposed enforcement method. Table 12 summarizes the ILV study, the validation studies, and the validation data submitted in conjunction with the field trial and processing studies.

Livestock: The petitioner is proposing a method developed by Ricerca, Inc. (Painesville, OH) for enforcement of the proposed livestock tolerances. The petitioner indicated that the LOQ and LOD for all analytes in the analyzed matrices are 0.01 and 0.005 ppm, respectively. A summary of the proposed enforcement method follows.

Residue Method for Determination of Bifenazate, D3598, A1530, and A1530-sulfate in Bovine Tissue and Milk: Milk, muscle, liver, and kidney samples are sequentially extracted with 100 ml of ACN and 100ml of ACN:water (1:1; contains 0.1% acetic acid). Fat samples are extracted with 100 ml of ACN (2x). The ACN extracts (fat) or the ACN and ACN:water extracts (milk, muscle, liver, and kidney) are combined and brought to a 250 ml volume with ACN.

For all matrices except fat, a 50 ml aliquot of the extract is hydrolyzed with 1.0 ml of concentrated HCl at 60 C for 2 hours (the hydrolysis step converts A1530-sulfate to A1530). The resulting hydrolysate is analyzed for A1530 via HPLC with fluorescence detection.

For all matrices, a 50 ml aliquot is partitioned with methylene chloride and 2% aqueous sodium sulfate. The methylene chloride phase is collected, evaporated to dryness, and the residue reconstituted with the HPLC mobile phase containing 0.05% ascorbic acid (the ascorbic acid reduces D3598 to bifenazate). After incubation for 2-6 hours, the extract is analyzed for bifenazate via HPLC with a oxidative coulometric electrochemical detection.

As stated earlier, the proposed livestock enforcement method was developed by Ricerca, Inc. (Painesville, OH). In support of the ILV requirement, the petitioner submitted MRID 45052224 (performed by the petitioner - Uniroyal Chemical Company, Inc. (Middlebury, CT)). The petitioner also submitted MRID 45052302 which provided validation data for the proposed enforcement method in/on tissues and milk (conducted by Ricerca, Inc. (Painesville, OH); October 1999). The analytical method used in the ruminant feeding study was the same as the proposed enforcement method except that residues of A1530 were determined in fat by analyzing an aliquot of the ACN extract using the A1530 HPLC method (hydrolysis step was not performed). Table 13 summarizes the ILV study, the validation study, and the validation data submitted in conjunction with the ruminant feeding study.

Table 11: Radioavalidation of Proposed Plant Enforcement Method

matrix	HPLC-RAD method; bifenazate + D3598		proposed enforcement method; bifenazate + D3598; ppm				ratio[2]	
	ppm	avg	uncorrected for recovery	corrected for recovery[1]	avg uncorr.	avg corr.	uncorr.	corr.
apple	0.186, 0.170	0.178	0.107, 0.117	0.127, 0.139	0.112	0.133	0.63	0.75
orange	0.342, 0.327	0.334	0.178, 0.196	0.225, 0.248	0.187	0.237	0.56	0.71

[1] concurrent recovery bifenazate and D3598 were 84% (apples) and 79% (oranges)
[2] residue from proposed enforcement method divided by residue determined by HPLC-RAD

Table 12: Validation Data for Proposed Plant Enforcement Method and Validation Data Submitted in Conjunction with the Field Trial and Processing Studies

matrix	fortification (ppm)	average % recovery ± std. dev.	
		bifenazate	D3598
MRID 45052311 (ILV study)			
apple	0.01, 0.1 (n=6)	90 ± 20	85 ± 4
MRID 45052314 (validation study)			
apple	0.01, 0.05, 0.1; (n=14)	91 ± 12	81 ± 10
orange	0.01, 0.05, 0.1; (n=14)	87 ± 7	87 ± 10
MRID 45052315 (validation study)[1]			
apple	0.025, 0.2; (n=10)	83 ± 9	94 ± 7
MRID 45052316 (validation study)			
apple	0.01, 0.1; (n=10)	90 ± 11	95 ± 8
orange	0.01, 0.1; (n=10)	88 ± 6	88 ± 10
MRID 45052317 (validation study)			
peach	0.01, 0.1, 1.0; (n=16)	78 ± 5	76 ± 3
plums	0.01, 0.1, 1.0; (n=16)	83 ± 7	81 ± 5
grapes	0.01, 0.1, 1.0; (n=16)	81 ± 7	74 ± 5
grape juice	0.01, 0.1, 1.0; (n=16)	95 ± 7	89 ± 6
raisin	0.01, 0.1, 1.0; (n=16)	80 ± 8	74 ± 8

matrix	fortification (ppm)	average % recovery ± std. dev.	
		bifenazate	D3598
prune	0.01 (n=8)	76 ± 4	**67 ± 3**
	0.1, 1.0; (n=8)	85 ± 5	80 ± 2
MRID 45052323 (hop magnitude of the residue study)			
hop	0.05 - 2.0 (n=9)	67, 69, 70-109	60, 65, 70-88
MRID 45052322 (grape magnitude of the residue study)			
grape	0.01 - 2.00 (n=21)	71-105	76-100
MRID 45052320 (apple magnitude of the residue study)			
apple	0.01 - 1.0 (n=9)	67, 69, 71-110, 150	--
MRID 45052321 (pear magnitude of the residue study)			
pear	0.01 - 1.0 (n=9)	120-120, 123	--
	0.5 (n=72)	--	92-120
MRID 45052326 (peach and plum magnitude of the residue and processing study)			
peach	0.01 - 1.00 (n=16)	64, 72-85	70-81
plum	0.01 - 1.00 (n=16)	72-101	73-89
prune	0.01 - 1.00 (n=16)	71-91	62, 66, 66, 67, 70-83
MRID 45076505 (strawberry magnitude of the residue study)			
strawberries	0.01 - 1.0 (n=9)	86-112	--
MRID 45052327 (cotton magnitude of the residue and processing study)			
cottonseed	0.01 - 1.00 (n=12)	72-98	76-94
gin byproduct	0.01 - 1.00 (n=12)	66, 68, 69, 75-106	72-114
meal	0.01 - 1.00 (n=12)	73-115	77-99
hulls	0.01 - 1.00 (n=12)	75-105	79-95
oil	0.01 - 1.00 (n=12)	69 (n=3), 68, 71-86	65, 75-116
MRID 45052324 (apple processing study)			
apple	0.01 - 1.0 (n=9)	74-104	--
apple juice	0.01 - 1.0 (n=9)	78-111	--
wet apple pomace	0.01 - 1.0 (n=9)	74-106	--
MRID 45052325 (grape processing and decline study)			
grape	0.01 - 1.0 (n=16)	72-99	66, 69, 70-84
grape juice	0.01 - 1.0 (n=16)	82-105	79-98
raisin	0.01 - 1.0 (n=16)	71-96	63-68 (n=6); 72-86

[1] the extracts from this study were not incubated with ascorbic acid (D3598 was not reduced to bifenazate); therefore, D3598 was quantified as D3598

Table 13: Validation Data for Proposed Livestock Enforcement Method and Validation Data Submitted in Conjunction with the Ruminant Feeding Study

matrix	fortification (ppm)	average % recovery ± std. dev.			
		bifenazate	D3598	A1530	A1530-S
MRID 45052302 (validation study)					
raw milk	0.01 (n=5)	95 ± 6	77 ± 9	100 ± 5	73 ± 3[1]
	0.1 (n=5)	96 ± 5	99 ± 6	106 ± 2	90 ± 9[1]
muscle	0.01 (n=5)	79 ± 4	75 ± 6	90 ± 9	**68 ± 6[1]**
	0.01 (n=5)	116 ± 8	103 ± 4	108 ± 10	82 ± 4[1]
liver	0.01 (n=5)	78 ± 1	**69 ± 8**	92 ± 5	95 ± 5
	0.1 (n=5)	96 ± 3	83 ± 3	92 ± 6	87 ± 4
kidney	0.01 (n=5)	93 ± 8	77 ± 4	104 ± 3	83 ± 7
	0.1 (n=5)	105 ± 2	83 ± 4	108 ± 2	87 ± 5
fat	0.01 (n=5)	77 ± 6	74 ± 7	99 ± 3	--
	0.1 (n=5)	94 ± 6	93 ± 4	97 ± 3	--
MRID 45052224 (ILV study)					
raw milk	0.01 (n=3)	**68 ± 12**	105 ± 8	86 ± 8	103 ± 4
	0.1 (n=3)	94 ± 6	90 ± 2	74 ± 2	92 ± 0.3
liver	0.01 (n=3)	85 ± 6	80 ± 7	89 ± 5	91 ± 3
	0.1 (n=3)	92 ± 4	**46 ± 20**	81 ± 7	82 ± 2
kidney	0.01 (n=3)	85 ± 12	83 ± 6	108 ± 4	**57 ± 5**
	0.1 (n=3)	**68 ± 3**	75 ± 18	84 ± 6	81 ± 4
fat	0.01 (n=3)	89 ± 1	111 ± 8	--	--
	0.1 (n=3)	102 ± 2	90 ± 8	--	--
MRID 45052304 (ruminant feeding study)					
milk	0.01 and 0.10 (n=28)	75 -111	64, 66, 66, 69, 69, 78-107	76-110	69, 71-106
butterfat	0.01 and 0.10 (n=4; n=3 for D3598 and A1530-sulfate)	81-92	71-86	67, 83-102	83-88
skin milk	0.01 and 0.10 (n=2)	86, 108	77, 98	90, 101	84, 100
loin muscle	0.01 or 0.10 (n=1)	99	85	99	85
round muscle	0.01 or 0.10 (n=1)	111	97	97	97
liver	0.01 or 0.10 (n=1)	88	84	87	91
kidney	0.10 (n=1)	100	81	104	72
ometnal fat	0.01 and 0.10 (n=3)	82-106	89-93	83-102	--
perirenal fat	0.01 and 0.10 (n=3)	93-117	86-97	94-108	--

[1] for A1530-S n=2

Conclusions: The analytical methods used in the field trial, processing, and ruminant feeding studies were the same as the proposed enforcement methods. Adequate validation was submitted with all of the studies excluding the apple field trial and processing studies and the strawberry field trial study. No validation data for determination of D3598 was submitted in conjunction with these studies. Since the method was validated for determination of D3598 in/on numerous fruit commodities, HED concluded that the method was adequately validated for determination of D3598 in/on apple, apple juice, apple pomace, and strawberry. The following paragraphs pertain to the plant and livestock enforcement methods.

Plant: The proposed plant enforcement method has been adequately radiovalidated and validated by an independent laboratory. HED forwarded the method to the Analytical Chemistry Laboratory (ACL) for PMV (D271330, T. Bloem, 21-Dec-2000). The petitioner will be required to make any modifications or revisions to the proposed enforcement method resulting from PMV. The petitioner is requested to submit a confirmatory method and an interference study. If the petitioner proposes a confirmatory method which employs a MSD, then an interference study is not necessary (chromatograms and spectra of fortified samples should be submitted; structurally significant ions should be chosen with a m/z > 91 and intensity > 3x noise at the LOQ for the primary method).

Livestock: The ILV study resulted in marginal recoveries of bifenazate (milk and kidney), D3598 (liver), and A1530-sulfate (kidney). HED forwarded the method to the ACL for further evaluation and, if appropriate, PMV (D271330, T. Bloem, 21-Dec-2000). The petitioner will be required to make any modifications or revisions to the proposed enforcement method resulting from ACL review and/or PMV. The petitioner is requested to submit radiovalidation of the proposed enforcement method, a confirmatory method, and an interference study. If the petitioner proposes a confirmatory method which employs a MSD, then an interference study is not necessary (chromatograms and spectra of fortified samples should be submitted; structurally significant ions should be chosen with a m/z > 91 and intensity > 3x noise at the LOQ for the primary method).

OPPTS GLN 860.1360: Multiresidue Method

The petitioner submitted data concerning the recovery of bifenazate and D3598 using FDA multiresidue method protocols A, C, D, E, and F (PAM Vol. I; MRID 45052318). These data were forwarded to FDA for inclusion in the Pesticide Analytical Manual I (D273067, T. Bloem, 6-Mar-2001). Due to instability in methanol, neither compound could be accurately quantified using Protocol A. Gas chromatographic systems equipped with a DB-1 type column and either an ECD or NPD detector gave acceptable results for both compounds (Protocol C). Recovery from apples using Protocol D without Florisil cleanup resulted in recoveries of ≤43%. Testing using Protocols E and F Florisil cleanup systems resulted in recoveries of <30%. The tolerance expression for livestock commodities includes A1530 and A1530-sulfate. The petitioner should submit information concerning the behavior of these compounds through the FDA multiresidue protocols.

OPPTS GLN 860.1380: Storage Stability Data

MRID 45052319 - Stability of D2341 and Metabolite in Fruit Matrices during Freezer Storage: Samples of peach, apple, orange, prune, grape juice, and grape were homogenized, fortified with bifenazate or D3598 at 0.10 ppm, and placed in frozen storage (-20 C). To determine surface residue stability, samples of unprocessed peach, grape, and apple were fortified with bifenazate or D3598 at 0.10 ppm and placed in frozen storage (-20 C). The stored samples were analyzed along with freshly fortified samples using the same method as the proposed enforcement method (LOQ = 0.01 ppm). The analytical method was adequately validated and residues in/on control samples were ≤0.01 ppm. Table 14 summarizes the frozen storage stability of bifenazate and D3598 in fruit.

MRID 45052327 - UCC-D2341 50WP on Cotton: Magnitude of the Residue and Processing Study: The cotton field trial and processing study also contained data concerning the storage stability of bifenazate and D3598 in/on cotton matrices. Untreated samples were fortified with bifenazate or D3598 at 0.1 ppm and placed in frozen storage (-20 C). The stored samples were analyzed along with freshly fortified samples using the same method as the proposed enforcement method (LOQ = 0.01 ppm). The analytical method was adequately validated and residues in/on control samples were <0.01 ppm. Table 14 summarizes the frozen storage stability of bifenazate and D3598 in cotton matrices.

MRID 45052303 - Stability of D2341 and Metabolites D3598 and A1530 in Bovine Tissues and Milk During Freezer Storage: Samples of bovine milk, muscle, liver, kidney, and fat were homogenized, fortified with bifenazate, D3598, or A1530 at 0.20 ppm, and placed in frozen storage (temperature was not provided). The stored samples were analyzed along with freshly fortified samples using the same method as the proposed enforcement method except that residues of A1530 were determined in fat by analyzing an aliquot of the ACN extract using the A1530 HPLC method (hydrolysis step was not performed). The method was adequately validated and residues in/on controls were <0.01 ppm. Table 15 summarizes the frozen storage stability of bifenazate, D3598, and A1530 in tissues and milk.

Table 14: Frozen Storage Stability of Bifenazate and D3598 in Fruit

matrix[1]	storage interval (days)	freshly fortified % recovery[2]		stored % recovery		corrected % recovery[3]	
		bifenazate	D3598	bifenazate	D3598	bifenazate	D3598
MRID 45052319							
apple (homogenized)	0	97, 109; 103	95, 97; 96	94, 92	95, 96	91, 89	99, 100
	7	91, 95; 93	94, 91; 93	78, 80	86, 81	84, 86	92, 87
	14	72, 69; 71	70, 78; 74	56, 57	65, 63	79, 80	88, 85
	21	68, 68; 68	63. 67; 65	46, 41	48, 48	**68, 60**	74, 74
	29	73, 77; 75	81, 81; 81	53, 58	65, 63	71, 77	80, 78
	42	67, 67; 67	68, 72; 70	52, 52	50, 48	78, 78	71, **69**
	70	91, 88; 90	86, 79; 83	57, 55	51, 56	**63, 61**	**61, 67**
	107	87, 88; 88	77, 81; 79	42, 42	41, 44	**48, 48**	**52, 56**
	182	89, 91; 90	79, 71; 75	38, 35	37, 41	**42, 39**	**49, 55**
apple (surface)	0	88, 90; 89	73, 76; 75	88, 93	77, 76	99, 104	103, 101
	14	81, 92; 87	81, 83; 82	88, 92	75, 90	104, 106	91, 110
	28	94, 88; 91	79, 79; 79	78, 90	80, 69	86, 99	101, 87
	56	88, 84; 86	89, 90; 90	98, 86	70, 68	114, 100	78, 76
	126	92, 87; 90	90, 83; 87	93, 96	73, 51	103, 107	84, **59**
	224	94, 92; 93	86, 80; 83	98, 88	72, 82	105, 95	87, 99
grapes (homogenized)	0	95, 99; 97	86, 86; 86	92, 90	88, 89	95, 93	102, 103
	7	90, 92; 91	89, 89; 89	66, 62	69, 73	76, **68**	78, 82
	14	81, 79; 80	73, 74; 74	51, 49	50, 49	**64, 61**	**68, 67**
	21	76, 79; 78	74, 75; 75	45, 35	39, 39	**58, 45**	**52, 52**
	29	81, 90; 86	82, 78; 80	46, 31	45, 44	**53, 36**	**56, 55**
	42	79, 72; 76	77, 74; 76	44, 31	31, 37	**58, 41**	**41, 49**
	70	87, 83; 85	85, 87; 86	23, 19	20, 24	**27, 22**	**23, 28**

matrix[1]	storage interval (days)	freshly fortified % recovery[2]		stored % recovery		corrected % recovery[3]	
		bifenazate	D3598	bifenazate	D3598	bifenazate	D3598
grape (surface)	0	100, 95; 98	86, 89; 88	71, 81	71, 76	72, 83	81, 86
	14	107, 98; 103	93, 92; 93	88, 88	86, 86	85, 85	92, 92
	28	94, 89; 92	84, 90; 87	83, 81	74, 74	90, 88	85, 85
	56	85, 87; 86	86, 90; 88	79, 70	79, 68	92, 81	90, 77
	126	96, 94; 95	94, 90; 92	81, 83	73, 78	85, 87	79, 85
	224	84, 97; 91	82, 84; 83	73, 76	66, 67	80, 84	80, 81
peach (homogenized)	0	91, 88; 90	90, 91; 91	89, 91	88, 92	99, 101	97, 101
	7	81, 84; 83	81, 79; 80	68, 67	70, 70	82, 81	88, 88
	14	81, 80; 81	96, 86; 91	58, 30	61, 67	72, 37	67, 74
	21	74, 79; 77	76, 67; 72	48, 53	49, 54	62, 69	68, 75
	28	71, 71; 71	68, 72; 70	49, 52	57, 59	69, 73	81, 84
	42	91, 84; 88	92, 89; 91	62, 56	63, 74	70, 64	69, 81
	70	84, 81; 83	86, 81; 84	47, 55	55, 57	57, 66	65, 68
	105	83, 85; 84	75, 82; 79	41	36, 33	49	46, 42
	182	87, 84; 86	77, 80; 79	33, 33	35, 37	38, 38	44, 47
peach (surface)	0	97, 93; 95	82, 86; 84	81, 86	67, 66	85, 91	80, 79
	14	98, 92; 95	80, 89; 85	75, 84	66, 72	79, 88	78, 85
	28	83, 78; 81	83, 74; 79	58, 59	50, 42	72, 73	63, 53
	56	91, 95; 93	79, 90; 85	60, 77	42, 44	65, 83	61, 52
	126	101, 88; 95	89, 82; 86	49, 62	35, 40	52, 65	41, 47
	223	98, 94; 96	77, 79; 78	63, 67	44, 56	66, 70	56, 72
orange (homogenized)	0	81, 89; 85	82, 85; 84	87, 84	86, 82	102, 99	102, 98
	7	79, 83; 81	78, 79; 79	63, 63	68, 71	78, 78	86, 90
	14	89, 88; 89	79, 74; 77	56, 66	61, 62	63, 74	79, 81
	28	92, 87; 90	81, 83; 82	70, 59	60, 76	78, 66	73, 93
	40	91, 92; 92	72, 69; 71	64, 62	69, 65	70, 67	97, 92
	75	95, 94; 95	87, 80; 84	66, 68	69, 72	69, 72	82, 86
	105	82, 87; 85	72, 71; 72	55, 50	58, 66	65, 59	81, 92
	186	95, 96; 96	81, 83; 80	52, 51	65, 68	54, 53	79, 83
grape juice	0	99, 98; 99	92, 93; 93	95, 95	89, 89	96, 96	96, 96
	7	99, 99; 99	87, 84; 86	89, 105	85, 87	90, 106	99, 101
	14	98, 95; 97	88, 88; 88	96, 98	84, 83	99, 101	95, 94
	28	94, 94; 94	86, 89; 88	96, 101	85, 82	102, 107	97, 93
	40	91, 90; 91	81, 80; 81	91, 89	81, 79	100, 98	100, 98
	75	97, 102; 100	90, 91; 91	103, 96	89, 84	103, 96	98, 92
	107	96, 94; 95	82, 77; 80	95, 95	87, 86	100, 100	109, 108
	186	99, 97; 98	83, 84; 84	104	85, 87	106	101, 104

matrix[1]	storage interval (days)	freshly fortified % recovery[2]		stored % recovery		corrected % recovery[3]	
		bifenazate	D3598	bifenazate	D3598	bifenazate	D3598
prunes (homogenized)	0	76, 72; 74	66, 67; 67	73, 72	72, 70	99, 97	107, 104
	7	76, 80; 78	71, 73; 72	75, 69	70, 68	96, 88	97, 94
	14	75, 73; 74	77, 81; 79	82, 73	63, 63	111, 99	80, 80
	28	83, 80; 82	78, 70; 74	73, 70	64, 61	89, 85	86, 82
	42	80, 85; 83	72, 79; 76	72, 73	57, 62	87, 88	75, 82
	70	86, 87; 87	75, 71; 73	67, 66	56, 52	77, 76	77, 71
	105	84, 84; 84	79, 71; 75	71, 68	56, 57	85, 81	75, 76
	182	86, 94; 90	70, 66; 68	80, 78	55, 53	89, 87	81, 78
MRID 45052327							
cottonseed	0	98	90	78, 100	93, 85	80, 103	104, 94
	21	99	88	38, 38	38, 46	38, 39	43, 53
	56	99	83	59, 67	40, 43	59, 68	48, 52
cotton gin byproduct	0	83	76	76, 76	73, 75	91, 92	96, 99
	44	79	84	51, 55	49, 41	64, 69	58, 49
hulls	0	77	83	89, 87	84, 83	115, 112	101, 100
	52	98	93	70, 63	67, 64	72, 64	72, 69
meal	0	99	88	95, 94	88, 91	96, 95	100, 103
	43	96	92	58, 55	71, 80	60, 58	76, 87
refined oil	0	70	79	55, 66	73, 77	78, 94	92, 97
	28	63	85	74, 77	72, 75	116, 122	84, 88

[1] all samples fortified at 0.10 ppm with either bifenazate or D3598

[2] individual recoveries followed by the average

[3] corrected for average recovery from freshly fortified samples; recoveries in bold are 130<x<70

Table 15: Frozen Storage Stability of bifenazate, D3598, and A1530 in Ruminant Milk and Tissue

storage interval (days)[1]	freshly fortified % recovery[2]			stored % recovery			corrected % recovery[3]		
	bifenazate	D3598	A1530	bifenazate	D3598	A1530	bifenazate	D3598	A1530
milk									
0	94, 96; 95	95, 94; 95	106, 106; 106	97, 97, 98, 94	101, 100, 97, 97	108, 109, 107, 109	102, 102, 103, 99	107, 106, 103, 103	102, 103, 101, 103
14	98, 103; 101	95, 99; 97	102, 105; 104	88, 93, 99, 96	93, 94, 95, 97	100, 99, 102, 102	88, 93, 99, 96	96, 97, 98, 100	97, 96, 99, 99
42	97, 92; 95	90, 87; 89	102, 100; 101	83, 84, 83, 85	83, 78, 81, 81	94, 89, 91, 92	88, 89, 88, 90	94, 88, 92, 92	93, 88, 90, 91
85	86, 86; 86	85, 85; 85	103, 101; 102	80, 79, 79, 83	73, 84, 79, 78	89, 90, 96, 92	93, 92, 92, 97	86, 99, 93, 92	87, 88, 94, 90
202	97, 96; 97	80, 76; 78	92, 97; 95	83, 79, 83, 81	78, 80, 79, 78	87, 81, 83, 81	86, 82, 86, 84	100, 103, 101, 100	92, 86, 88, 86
muscle									
0	106, 106; 106	96, 81; 89	91, 101; 96	107, 104, 104, 105	90, 82, 86, 98	97, 94, 98, 94	101, 98, 98, 99	102, 93, 97, 111	101, 98, 102, 98
2	84, 82; 83	82, 84; 83	na	49, 52, 47, 53	61, 59, 60, 61	na	**59, 63, 57, 64**	73, 71, 72, 73	na
14	102, 102; 102	103, 82; 93	103, 103; 103	65, 39, 45, 46	11, 30, 14, 7	91, 90, 90, 90	**64, 38, 44, 45**	**13, 32, 15, 8**	88, 87, 87, 87
28	98, 98; 98	91, 89; 90	93, 92; 93	22, 20, 20, 22	0, 0, 0, 0	80, 74, 77, 80	**22, 20, 20, 22**	**0, 0, 0, 0**	86, 80, 83, 86
86	na	na	96, 101; 99	na	na	67, 67, 68, 70	na	na	**68, 68, 69,** 71
liver									
0	98, 98; 98	79, 82; 81	95, 93; 94	99, 96, 99, 97	81, 79, 85, 88	95, 96, 95, 94	101, 98, 101, 99	101, 98, 106, 109	101, 102, 101, 100
2	72, 75; 74	78, 74; 76	102, 95; 99	18, 15, 30, 37	7, 7, 10, 6	88, 92, 93, 90	**24, 20, 41, 50**	**9, 9, 13, 8**	89, 93, 94, 91
14	105, 106; 106	88, 96; 92	97, 99; 98	92, 89, 88, 89	16, 18, 17, 13	86, 90, 89, 85	87, 84, 83, 84	**17, 20, 18, 14**	88, 92, 91, 87
kidney									
0	84, 92; 88	52, 54; 53	87, 89; 88	92, 90, 91, 95	57, 55, 62, 62	89, 90, 93, 96	105, 102, 103, 108	108, 104, 117, 117	101, 102, 106, 109
2	70, 74; 72	64, 74; 69	96, 102; 99	42, 34, 63, 45	13, 19, 31, 19	71, 82, 79, 79	**58, 47,** 88, **63**	**19, 28, 45, 28**	72, 83, 80, 80
14	93, 98; 96	79, 80; 80	101, 101; 101	64, 63, 60, 56	0, 0, 6, 0	65, 64, 68, 68	**67, 66, 63, 59**	**0, 0, 8, 0**	**64, 63, 67, 67**
fat									
0	87, 88; 88	86, 85; 86	111, 102; 107	91, 83, 85, 91	90, 87, 89, 90	105, 103, 104, 109	104, 95, 97, 104	105, 102, 104, 105	99, 97, 98, 102
14	73, 77; 75	80, 71; 76	104, 102; 103	62, 62, 64, 57	73, 79, 75, 68	84, 82, 82, 89	83, 83, 85, 76	97, 105, 99, 90	82, 80, 80, 86
36	93, 92; 92	76, 86; 81	108, 111; 110	75, 73, 73, 73	76, 81, 74, 85	90, 82, 87, 78	81, 79, 79, 79	94, 100, 91, 105	82, 75, 79, 71
95	113, 94; 104	84, 81; 83	107	69, 70, 68, 73	79, 78, 81, 74	82, 78, 70, 72	67, 68, 66, 71	96, 95, 98, 90	77, 73, 65, 67

[1] all samples fortified at 0.20 ppm with either bifenazate or D3598

[2] individual recoveries followed by the average

[3] corrected for average recovery from freshly fortified samples; recoveries in bold are 130<x<70

Conclusions: The plant and livestock storage stability data included with this petition are adequate. The following paragraphs summarize the results from these studies.

Plant: The storage stability data indicate that residues of bifenazate and D3598 are stable in/on homogenized frozen (-20 C) apple, grape, peach, orange, grape juice, and prunes for 42, 7, 42, 75 (186 days for D3598), 186, and 182 days, respectively. The stability of surface residues was evaluated by fortifying unhomogenized apple, grape, and peach with bifenazate and D3598. The resulting data indicate that surface bifenazate and D3598 residues were stable for 224 days on frozen (-20 C) apple and grape (longest interval tested) but were only stable for 14 days on peach (56 days for bifenazate). The cotton storage stability data are adequate and indicate that residues of bifenazate and D3598 are stable in frozen (-20 C) cottonseed hulls and oil for 52 and 28 days, respectively (longest interval tested). In cottonseed meal, D3598 was stable for 43 days but bifenazate was not stable for 43 days (43 days was the shortest interval tested for cottonseed meal). Bifenazate and D3598 were not stable for the shortest interval tested in cottonseed (21 days) and cotton gin byproduct (44 days).

The storage stability data validates the storage interval and conditions for the apple field trial study, grape field trial and processing studies, and the plum processing study. Since none of the currently available data can be translated to hops, HED requests the petitioner to validate the 175 day storage interval for dried hops (7-day interval from homogenization to analysis should also be validated). Since the storage interval for apple juice (295 days) and wet apple pomace (295 days) was greater than any validated interval, HED requests storage stability data for these commodities. Since the surface stability of D3598 on peach was 14 days, HED requests the petitioner to validate the 175 day storage interval for strawberry (5-day interval from homogenization to analysis should also be validated). The storage intervals for pear (field trial), peach and plum (field trial), and cotton (field trial and processing study) were not validated by the available storage stability data and the following paragraphs address this issue.

Pear: The pear field trial samples (MRID 45052321) were placed in frozen storage within 2 hours of collection, were homogenized within 60 - 120 days of collection, and were analyzed within 430 days of homogenization. Along with the pear field trial data, the petitioner presented stability data for a sample which was analyzed 60 days after collection (1 day after homogenization; 0.050 ppm) and analyzed a second time 468 days after collection (408 days after homogenization; 0.048 ppm). This information, combined with the fact that the combined residues of bifenazate and D3598 in/on pear were comparable to that found in/on apple, allowed for HED to conclude that the storage stability of the pear field trial samples had been adequately validated.

Peach and Plum (field trial): The samples were analyzed within 32 days of collection (within 11 days of homogenization; storage stability data for these intervals are marginal). The majority of the samples were analyzed within the validated storage interval of 14 days of collection and within 7 days of homogenization. Of the data which was not analyzed within the validated time intervals, only a single sample was collected 3 days after application (peach - Wharton, TX; 3 day PHI is requested; analyzed within 32 days of harvest, 5 days after homogenization). Since the combined bifenazate and D3598 residue from this sample was 2x greater than the residues from the other 3-day PHI samples and the storage stability data for homogenized peach was marginal when stored for 42 days (bifenazate - 64% and 70%; D3598 - 69% and 81%), HED concludes that the residue data from this site are acceptable.

Cotton: The cottonseed, cotton gin byproduct, cottonseed hull, cottonseed meal, and cottonseed refined oil samples samples were stored frozen for a maximum of 56, 42, 47, 39, and 48 days, respectively. The storage stability data indicate that residues of bifenazate and D3598 were not stable in/on cottonseed, cotton gin byproduct, and meal (21, 44, and 43 days, respectively, were the

shortest interval tested) and were stable in/on hulls and refined oil for 52 and 28 days, respectively (longest interval tested). Since the cotton was being harvested on different days and coordination with the processor and analytical laboratory were required, HED concludes that the interval from harvest or collection to analysis (maximum of 56 days) was reasonable and will not invalidate the data due to the lack of stability of bifenazate and D3598. However, correction factors of 0.57, 0.60, and 0.70 will be applied to the cottonseed, cotton gin byproduct, and cottonseed meal residue data, respectively (storage interval for cottonseed hulls and oil have been validated; therefore no correction factor will be applied to these commodities). The correction factors were based on the average recoveries of bifenazate and D3598 from the storage stability study.

Livestock: The storage stability data indicate that residues of bifenazate, D3598, and A1530 were stable in frozen (temperature was not provided) milk and fat for 298 and 95 days, respectively (longest interval tested). Residues of bifenazate and D3598 were not stable in frozen (temperature was not provided) muscle, liver, and kidney as the recoveries dropped below 70% after 2 days of storage (residues of D3598 were stable in muscle for 2 days but not 14 days). Residues of A1530 were stable in frozen (temperature was not provided) muscle, liver, and kidney for 28, 14, and 2 days, respectively.

In the ruminant feeding study, loin muscle, round muscle, liver, and kidney samples were analyzed within 1 day of collection and omental fat, perirenal fat, milk, butterfat, and skim milk samples were analyzed within 15, 15, 123, 46, and 103 days of collection, respectively. Adequate storage stability data has been submitted validating these storage intervals.

OPPTS GLN 860.1480: Meat/Milk/Poultry/Eggs

MRID 45052304 - Meat and Milk Magnitude of the Residue Study in Lactating Dairy Cows Dosed with D2341 Technical: The in-life and analytical portions of the study were conducted by Bio-Life Associates, Ltd. (Neillsville, WI) and the analytical portion of the study was conducted by Ricerca, Inc. (Painseville, OH). Lactating cows were orally dosed, for 28 consecutive days, with capsules containing bifenazate (dosed in the morning). Based on feed consumption (wet feed weights) and dosing rate, dietary burdens of 1 ppm (0.2x MTDB), 3 ppm (0.5x MTDB), and 10 ppm (1.7x MTDB) were calculated. Milk was collected in the a.m. and p.m. and pooled. Milk from test days 20 and 28 were separated into cream and skim milk. The cows were sacrificed 23 hours after the last dose and liver, kidney, round muscle, loin muscle, omental fat, and perirenal fat were collected. The samples were frozen upon collection and shipped to the analytical laboratory for analysis. The analytical method was the same as the proposed enforcement method except that residues of A1530 were determined in fat by analyzing an aliquot of the ACN extract using the A1530 HPLC method (no hydrolysis was performed; therefore, A1530-sulfate was not quantified). The method has been adequately validated and residues of bifenazate/D3598 and A1530/A1530-sulfate were <0.01 ppm in/on all control samples. Loin muscle, round muscle, liver, and kidney samples were analyzed within 1 day of collection and omental fat, perirenal fat, milk, butterfat, and skim milk samples were analyzed within 15, 15, 123, 46, and 103 days, respectively. Adequate storage stability data has been submitted validating these storage intervals. Table 16 summarizes the residues in/on the treated livestock commodities and Table17 summarizes the MTDB calculations.

Table 16: Bifenazate Residues in Dairy Cattle Commodities Following Oral Administration of Bifenazate

	dosing group	ppm	
		bifenazate/D3598[1]	A1530/A1530-sulfate[1]
milk	10 ppm (day 1-28)[2]	<0.01	<0.01
butter fat	10 ppm (day 20)	0.01	<0.01
	10 ppm (day 28)	0.03	<0.01
	3 ppm (day 20)	<0.01	<0.01
	3 ppm (day 28)	<0.01	<0.01
skim milk	10 ppm (day 20)	<0.01	<0.01
	10 ppm (day 28)	<0.01	<0.01
loin muscle	10 ppm	<0.01	<0.01
round muscle	10 ppm	<0.01	<0.01
liver	10 ppm	<0.01	<0.01
kidney	10 ppm	0.01	<0.01
omental fat[3]	10	0.07	<0.01
	3	0.02	<0.01
	1	<0.01	<0.01
perirenal fat[3]	10	0.10	<0.01
	3	0.03	<0.01
	1	<0.01	<0.01

[1] combined bifenazate/D3598 expressed as bifenazate; combined A1530/A1530-S expressed as A1530

[2] only 10 ppm milk samples were analyzed and all were <LOQ (LOQ = 0.01 ppm)

[3] fat samples were not analyzed for A1530-sulfate

Table 17: MTDB

	commodity	feedstuff	tolerance[1]	% DM[2]	% of diet	ppm in diet[3]
beef cattle	cotton	seed	0.5	88	20	0.11
	cotton	gin byproduct	20	90	20	4.44
	cotton	hulls	0.5	90	20	0.11
	apple	wet pomace	1.2	40	40	1.20
	MTDB					5.87
dairy cattle	cotton	seed	0.5	88	25	0.14
	cotton	gin byproduct	20	90	20	4.44
	cotton	hulls	0.5	90	15	0.08
	cotton	meal	0.5	89	15	0.08
	apple	wet pomace	1.2	40	20	0.60
	MTDB					5.35
poultry	cotton	meal	0.5	--	20	0.10
	MTDB					0.10
hog	cotton	meal	0.5	--	15	0.08
	MTDB					0.08

[1] recommended tolerance

[2] % dry matter

[3] (tolerance ÷ %DM) * % of diet; for poultry and hog no correction for %DM

Conclusions: Lactating cows were orally administered bifenazate for 28 consecutive days at feeding levels of 1 ppm (0.2x maximum theoretical dietary burden (MTDB)), 3 ppm (0.5x MTDB), or 10 ppm (1.7x MTDB). Milk was collected in the a.m. and p.m. and pooled. The cows were sacrificed 23 hours after the last dose and liver, kidney, round muscle, loin muscle, omental fat, and perirenal fat were collected. Residues of bifenazate/D3598 and A1530/A1530-sulfate were <0.01 ppm in liver, muscle, skim milk, and milk collected from the 10 ppm dosing group. Residues of bifenazate/D3598 were found in butter fat (10 ppm dosing group - 0.01 ppm and 0.03 ppm), kidney (10 ppm dosing group - 0.01 ppm), omental fat (10 ppm dosing group - 0.07 ppm; 3 ppm dosing group - 0.02 ppm), and perirenal fat (10 ppm dosing group - 0.10 ppm; 3 ppm dosing group - 0.03 ppm). Residues of A1530/A1530-sulfate were <0.01 ppm in kidney, butter fat, omental fat, and perirenal fat samples collected from the 10 ppm dosing group. Generally, HED requires a feeding study conducted at 10x the MTDB. For the purposes of this petition, HED will accept the submitted feeding study but advises the petitioner that if the dietary burden increase as a result of additional uses, then a new feeding study may be requested.

Based on the ruminant feeding study and the MTDB for ruminants, HED concludes that the following tolerances for the combined residue of bifenazate, D3598 (expressed as bifenazate), A1530, and A1530-sulfate (expressed as A1530) are appropriate: milk - 0.01 ppm; meat (cattle, goat, hog, horse, and sheep) - 0.01 ppm; meat byproducts (cattle, goat, hog, horse, and sheep) - 0.01 ppm; and fat (cattle, goat, hog, horse, and sheep) - 0.10 ppm (tolerance expression for fat includes only bifenazate and D3598 (expressed as bifenazate)). The petitioner should submit a revised Section F.

Based on the poultry MTDB and the residues identified in the poultry metabolism study, HED concludes that there is no reasonable expectation of finite residues in poultry commodities and will not request a poultry feeding study (category 180.6(a)(3)). The use of the poultry metabolism study in lieu of a feeding study is appropriate for this petition only. If in the future the dietary burden to poultry increases, a poultry feeding study may be required.

OPPTS GLN 860.1500: Crop Field Trials

Pome Fruit

MRID 48052322 - UCC-D2341 50WP on Apples: Magnitude of the Residue and MOR Decline Study: The in-life phase of the study was conducted by several companies and the analytical portion of the study was conducted by Uniroyal Chemical Co. (Guelph, Ontario). A total of 12 test sites were established during 1998 in North Rose, NY (Region 1); Hereford, PA (Region 1); Winterville, GA (Region 2); Conklin, MI (Region 5); Orchard City, CO (Region 9); Sebastopol, CA (Region 10); Wapato, WA (Region 11); Monitor, WA (Region 11); Hood River, OR (Region 11); The Dalles, OR (Region 11); Dundee, NY (Region 1); and Ephrata, WA (Region 11). Each site consisted of a treated and a control plot. The treated plots received a single application of a 50WP formulation of bifenazate at ~0.50 lbs ai/acre (1x proposed seasonal rate). Applications were made with airblast equipment with spray volumes of ~50 gallons/acre. Single control and duplicate treated samples were collected by hand at maturity 7, 14, and 21 days after treatment. At some of the sites, samples were also collected 3 and 28 days after treatment. The samples were placed in frozen storage within 3 hours of collection, shipped to the analytical laboratory, and analyzed within 197 days of collection (within 12 days of homogenization; adequate storage stability data validates this interval). The analytical method was the same as the proposed enforcement method. Validation of the method for determination of bifenazate in/on apples was performed and resulted in adequate recoveries. Validation of the method for determination of D3598 in/on apples was not performed in conjunction with this study. However, the method has been previously validated for determination of D3598 in/on apple and is therefore considered to be adequately validated (LOQ = 0.01 ppm). The combined residues of bifenazate/D3598 were <0.01 ppm in/on 43 of the 46 control samples (0.02, 0.07, and 0.01 ppm). Table 18 summarizes the residues of bifenazate/D3598 in/on treated apples.

Table 18: Residues of bifenazate/D3598 in/on Apple

site	treatment rate (lbs ai/acre)	PHI (days)	combined bifenazate/D3598 (ppm)[1]
Hereford, PA (Region 1)	0.50	7	0.58, 0.57 **HAFT = 0.58**
		14	0.36, 0.36
		21	0.08, 0.09
	0.50	7	0.20, 0.20
		14	0.12, 0.14
		21	0.10, 0.05
North Rose, NY (Region 1)	0.50	7	0.06, 0.06
		14	0.01, 0.01
		21	0.14, 0.14
Dundee, NY (Region 1)	0.50	3	0.10, 0.11
		7	0.19, 0.18
		14	0.13, 0.12
		21	0.12, 0.14
		28	0.15, 0.14
Winterville, GA (Region 2)	0.49	7	0.16, 0.16
		14	0.08, 0.02
		21	0.08, 0.09
Conklin, MI (Region 5)	0.50	7	0.13, 0.17
		14	0.15, 0.02
		21	0.10, 0.10
	0.50	7	0.22, 0.22
		14	0.20, 0.20
		21	0.11, 0.11
Orchard City, CO (Region 9)	0.50	7	0.19, 0.26
		14	0.20, 0.20
		21	0.02, 0.02
Sebastopol, CA (Region 10)	0.52	7	0.19, 0.17
		14	0.17, 0.17
		21	0.11, 0.10
Wapato, WA (Region 11)	0.49	7	0.16, 0.19
		14	0.25, 0.04
		21	0.07, 0.08

site	treatment rate (lbs ai/acre)	PHI (days)	combined bifenazate/D3598 (ppm)[1]
Monitor, WA (Region 11)	0.50	7	0.37, 0.37
		14	0.15, 0.15
		21	0.17, 0.16
Hood River, OR (Region 11)	0.48	7	0.18, 0.15
		14	0.12, 0.13
		21	0.08, 0.08
The Dalles, OR (Region 11)	0.49	7	0.06, 0.04
		14	0.02, 0.02
		21	0.02, 0.02
Ephrata, WA (Region 11)	0.50	3	0.45, 0.50
		7	0.38, 0.38
		14	0.36, 0.36
		21	0.25, 0.24
		28	0.22, 0.21

[1] combined bifenazate/D3598 residues expressed as bifenazate

MRID 48052321 - Bifenazate 50WP on Pears: Magnitude of the Residue Study: The in-life phase of the study was conducted by several companies and the analytical portion of the study was conducted by Uniroyal Chemical Co. (Guelph, Ontario). A total of 8 test sites were established during 1998 in Alton, NY (Region 1); Orefield, PA (Region 1); Fairfield, CA (Region 10); Upper Lake, CA (Region 10); Zillah, WA (Region 11); Soap Lake, WA (Region 11); Naches, WA (Region 11); and Hood River, OR (Region 11). Each site consisted of a treated and a control plot. The treated plots received a single application of a 50WP formulation of bifenazate at ~0.50 lbs ai/acre (1x proposed seasonal rate). Applications were made with airblast equipment with spray volumes of ~50 gallons/acre. Single control and duplicate treated samples were collected by hand 7, 14, and 21 days after treatment. The samples were placed in frozen storage within 2 hours of collection and shipped to the analytical laboratory for analysis. The analytical method was the same as the proposed enforcement method and has been adequately validated (LOQ = 0.01 ppm). The samples were homogenized within 2 - 4 months of collection and were analyzed within 430 days of homogenization. This storage interval has not been validated. In conjunction with the field trial data, the petitioner submitted storage stability data for a sample collected from Hood River OR (21 day PHI). The sample was initially analyzed 60 days after collection (1 day after homogenization; 0.050 ppm) and analyzed a second time 468 days after collection (408 days after homogenization; 0.048 ppm). This data, combined with the fact that the pear residue data was similar to the apple residue data, allowed HED to conclude that the storage stability of the pear samples has been validated. The combined residues of bifenazate/D3598 were <0.01 ppm in/on 21 of the 24 control samples collected (0.01, 0.01, and 0.01 ppm). Table 19 summarizes the residues of bifenazate/D3598 in/on treated pears.

Table 19: Residues of bifenazate/D3598 in/on Pear

site	treatment rate (lbs ai/acre)	PHI (days)	combined bifenazate/D3598 (ppm)[1]
Alton, NY (Region 1)	0.50	7	0.11, 0.09
		14	0.03, 0.04
		21	0.02, 0.03
Orefield, PA (Region 1)	0.50	7	0.25, 0.23
		14	0.08, 0.08
		21	0.12, 0.10
Fairfield, CA (Region 10)	0.50	7	0.14, 0.13
		14	0.04, 0.03
		21	0.02, 0.02
Upper Lake, CA (Region 10)	0.50	7	0.05, 0.10
		14	0.16, 0.10
		21	0.08, 0.09
Zillah, WA (Region 11)	0.49	7	0.15, 0.16
		14	0.13, 0.12
		21	0.13, 0.12
Soap Lake, WA (Region 11)	0.50	7	0.11, 0.07
		14	0.07, 0.04
		21	0.04, 0.10
Hood River, OR (Region 11)	0.50	7	0.09, 0.10
		14	0.10, 0.09
		21[2]	0.05
		21[2]	0.04, 0.04
Naches, WA (Region 11)	0.48	7	0.28, 0.30
		14	0.17, 0.21
		21	0.12, 0.08

[1] combined bifenazate/D3598 residues expressed as bifenazate

[2] stability data for a sample which was analyzed 60 days after collection (1 day after homogenization) and analyzed a second time 468 days after collection (408 days after homogenization)

Conclusion: The petitioner submitted apple magnitude of the residue data conducted in Region 1 (n=3), Region 2 (n=1), Region 5 (n=1), Region 9 (n=1), Region 10 (n=1), and Region 11 (n=5) and pear magnitude of the residue data conducted in Region 1 (n=2), Region 10 (n=2), and Region 11 (n=4). A single application of a 50WP formulation of bifenazate was applied to apple and pear trees at 1x the maximum proposed seasonal application rate. Apples were harvested 7, 14, and 21 days after application and the combined residues of bifenazate/D3598 ranged from 0.04 - 0.58 ppm, 0.01 - 0.36 ppm, and 0.01 - 0.25 ppm, respectively (7-day PHI requested). Pears were harvested 7, 14, and 21 days after application and the combined residues of bifenazate/D3598 ranged from 0.05 - 0.30 ppm, 0.03 - 0.21 ppm, and 0.02 - 0.13 ppm, respectively (7-day PHI requested). In general, residues decreased as the PHI increased from 7 to 21 days.

Tables 2 and 5 of OPPTS GLN 860.1500 suggests the following field trial data when requesting a tolerance in/on pome fruit: apple - Region 1 (n=3), Region 2 (n=1), Region 5 (n=2), Region 9 (n=1), Region 10 (n=1), and Region 11 (n=4) and pear - Region 1 (n=1), Region 10 (n=2), and Region 11 (n=3). The geographical distribution of the pear field trial data is adequate. An apple field trial in Region 5 is needed to fulfill the suggested geographical distribution. Since the petitioner conducted an additional apple field trial in Region 11, no additional field trial data will be requested. HED concludes that the available data support the petitioner proposed tolerance of 0.75 ppm for the combined residues of bifenazate and D3598 (expressed as bifenazate) in/on pome fruit. However, the preferred commodity term is "fruit, pome, group." The petitioner should submit a revised Section F.

Stonefruit

MRID 45052326 - UCC-D2341 50WP on Stonefruit: Magnitude of the Residue and Processing Study: The in-life phase of the study was conducted by several companies and the analytical portion of the study was conducted by Ricerca, Inc. (Painesville, OH). A total of 10 peach test sites were established during 1998 in Hereford, PA (Region 1); Saluda County, SC (Region 2); Aiken County, SC (Region 2); Winterville, GA (Region 2); Conklin, MI (Region 5); Wharton, TX (Region 6); Madera, CA (Region 10); Lemoore, CA (Region 10); Fairfield, CA (Region 10); and Escalon, CA (Region 10). A total of 7 plum test sites were established in 1998 in Conklin, MI (Region 5); Madera, CA (Region 10); Ivanhor, CA (Region 10); Davis, CA (Region 10); Marysville, CA (Region 10); Dallas, OR (Region 12); and Toppenish, WA (Region 11). Each site consisted of a treated and a control plot. The treated plots received a single application of a 50WP formulation of bifenazate at ~0.50 lbs ai/acre (1x proposed seasonal rate). Applications were made with airblast equipment with spray volumes of ~50 gallons/acre. Single control and duplicate treated samples were collected by hand at maturity 3, 7, and 14 days after treatment. At some of the sites, samples were also collected 1 and 21 days after treatment. The samples were placed in frozen storage within 3 hours of collection, shipped to the analytical laboratory, and analyzed within 32 days of collection (within 11 days of homogenization; storage stability data for this interval is marginal). The majority of the samples were analyzed within the validated storage interval of 14 days of collection and within 7 days of homogenization. Of the data which was not analyzed within the validated time intervals, only a single sample was collected 3 days after application (peach - Wharton, TX; 3 day PHI is requested; analyzed within 32 days of harvest, within 5 days of homogenization). Since the combined bifenazate and D3598 residue from this sample was 2x greater than the residues from the other 3-day PHI samples and the storage stability data for homogenized peach was marginal when stored for 42 days (bifenazate - 64% and 70%; D3598 - 69% and 81%), HED concluded that the residue data from this site was acceptable. The analytical method was the same as the proposed enforcement method and has been adequately validated (LOQ = 0.01 ppm). The combined residues of bifenazate/D3598 were <0.01 ppm in/on all of the control samples. Table 20 summarizes the residues of bifenazate/D3598 in/on treated plums.

Table 20: Residues of bifenazate/D3598 in/on Peaches and Plums[1]

site	treatment rate (lbs ai/acre)	PHI (days)	combined bifenazate/D3598[2] (ppm)
peach			
Hereford, PA (Region 1)	0.50	3	0.53, 0.57
		7	0.26, 0.40
		14	0.24, 0.13
Saluda County, SC (Region 2)	0.49	3	0.22, 0.23
		7	0.12, 0.16
		14	0.15, 0.09
Aiken County, SC (Region 2)	0.49	3	0.23, 0.22
		7	0.20, 0.15
		14	0.13, 0.15
Winterville, GA (Region 2)	0.50	3	0.14, 0.20
		7	0.10, 0.12
		14	0.07, 0.04
Conklin, MI (Region 5)	0.49	3	0.27, 0.17
		7	0.18, 0.19
		14	0.06, 0.04
Wharton, TX (Region 6)	0.50	3	*1.02, 1.45*
		7	*1.44, 0.57*
		14	*0.55, 0.90*
Madera, CA (Region 10)	0.51	1	0.43, 0.49
		3	0.38, 0.41
		7	0.22, 0.30
		14	*0.20, 0.14*
		21	0.21, 0.17
Lemoore, CA (Region 10)	0.51	3	0.10, 0.19
		7	0.10, 0.21
		14	0.13, 0.06
Fairfield, CA (Region 10)	0.51	3	0.15, 0.11
		7	0.08, 0.11
		14	0.03, 0.03

site	treatment rate (lbs ai/acre)	PHI (days)	combined bifenazate/D3598[2] (ppm)
Escalon, CA (Region 10)	0.50	4	0.24, 0.28
		7	*0.12, 0.12*
		14	0.09, 0.09
plums			
Conklin, MI (Region 5)	0.50	3	0.15, 0.10
		7	0.08, 0.07
		14	0.04, 0.05
Madera, CA (Region 10)	0.51	3	0.01, 0.01
		7	<0.01, <0.01
		14	<0.01, <0.01
Ivanhoe, CA (Region 10)	0.50	3	0.04, 0.03
		7	0.02, 0.02
		14	0.01, 0.01
Davis, CA (Region 10)	0.50	1	*0.06, 0.07*
		3	0.06, 0.06
		7	0.04, 0.03
		14	0.05, 0.03
		21	0.02, 0.02
Marysville, CA (Region 10)	0.50	3	0.04, 0.03
		7	0.04, 0.03
		14	0.01, 0.02
Dallas, OR (Region 12)	0.50	1	0.03, 0.04
		3	0.03, 0.03
		7	0.02, 0.02
		14	0.01, 0.02
		21	0.01, 0.01
Toppenish, WA (Region 11)	0.51	3	0.03, 0.04
		7	0.03, 0.02
		14	0.01, 0.01

[1] residues in italics indicates storage intervals which were not adequately validated (unhomogenized sample stored for >14 days and/or homogenized sample stored for >7 days)

[2] combined bifenazate/D3598 residues expressed as bifenazate

Conclusion: The petitioner submitted peach magnitude of the residue data conducted in Region 1 (n=1), Region 2 (n=3), Region 5 (n=1), Region 6 (n=1), and Region 10 (n=4) and plum magnitude of the residue data conducted in Region 5 (n=1), Region 10 (n=4), Region 11 (n=1), and Region 12 (n=1). A single application of a 50WP formulation of bifenazate was applied to peach and plum trees at 1x the maximum proposed seasonal application rate. Peaches were harvested 3, 7, and 14 days after application and the combined residues of bifenazate/D3598 ranged from 0.10 - 1.45 ppm, 0.08 - 1.44 ppm, and 0.03 - 0.90 ppm, respectively (3-day PHI requested). Plums were harvested 3, 7, and 14 days after application and the combined residues of bifenazate/D3598 ranged from 0.01 - 0.15 ppm, <0.01 - 0.08 ppm, and <0.01 - 0.05 ppm, respectively (3-day PHI requested).

Tables 2 and 5 of OPPTS GLN 860.1500 suggests the submission of the following field trial data when requesting a tolerance in/on stonefruit: cherry (sweet) - Region 5 (n=2), Region 10 (n=2), and Region 11 (n=2) or cherry (tart) - Region 1 (n=1), Region 5 (n=4), and Region 9 (n=1); peach - Region 1 (n=1), Region 2 (n=3), Region 5 (n=1), Region 6 (n=1), and Region 10 (n=3); and plum - Region 5 (n=1), Region 10 (n=4), and Region 12 (n=1). Since the petitioner has not submitted any cherry field trial data and the maximum peach (1.45 ppm) and plum (0.15 ppm) residue varied by a factor greater than 5x, a stonefruit crop group tolerance is not appropriate and the 25% reduction in the number of field trials when receiving a crop group tolerance does not apply.

Currently, the petitioner is requesting registration for application to peach, nectarine, apricot, and plum. To establish registration on these crops, Table 5 of OPPTS GLN 860.1500 suggests the following geographical field trial distribution: peach - Region 1 (n=1), Region 2 (n=4), Region 4 (n=1), Region 5 (n=1), Region 6 (n=1), and Region 10 (n=4); apricot - Region 10 (n=4) and Region 11 (n=1); and plum - Region 5 (n=1), Region 10 (n=5), Region 11 (n=1), and Region 12 (n=1). The geographical distribution of the field trial data is insufficient and the petitioner should submit the following field trial data: peach - Region 2 (n=1) and Region 4 (n=1); plum - Region 10 (n=1); apricot - Region 10 (n=4) and Region 11 (n=1). Since no apricot field trial data have been submitted, an apricot registration is not appropriate (directions for application to apricots should be removed from the label). Provided the petitioner agrees to submit the requested peach and plum field trial data, HED concludes that the available data support a plum tolerance of 0.30 ppm and a peach tolerance of 1.7 ppm for the combined residue of bifenazate and D3598 (expressed as bifenazate). The petitioner should submit a revised Section F.

Grape

MRID 48052322 - UCC-D2341 50WP on Grapes: Magnitude of the Residue Study: The in-life phase of the study was conducted by several companies and the analytical portion of the study was conducted by Ricera, Inc. (Painseville, OH). A total of 11 test sites were established during 1998 in Dundee, NY (Region 1); Fresno, CA (Region 10); Kerman, CA (Region 10); Tulare, CA (Region 10); Suisan, CA (Region 10); Ripon, CA (Region 10); Upper Lake, CA (Region 10); Linden, CA (Region 10); Hughson, CA (Region 10); Granger, WA (Region 11); and George, WA (Region 11). Each site consisted of a treated and a control plot. The treated plots received a single application of a 50WP formulation of bifenazate at ~0.50 lbs ai/acre (1x proposed seasonal rate). Applications were made with airblast equipment with spray volumes of ~50 gallons/acre. Single control and duplicate treated samples were collected by hand at maturity 14 and 21 days after treatment. The samples were placed in frozen storage within 1 hour of collection, shipped to the analytical laboratory, and analyzed within 20 days of collection (within 1 day of homogenization; adequate storage stability data validates this interval). The analytical method was the same as the proposed enforcement method and has been adequately validated (LOQ = 0.01 ppm). The combined residues of bifenazate/D3598 were <0.01 ppm in/on all control samples except for 1 sample collected from at the Granger, WA site which had a residue of 0.06 ppm. Table 21 summarizes the residues of bifenazate/D3598 in/on treated grapes.

Table 21: Residues of bifenazate/D3598 in/on Grapes

site	treatment rate (lbs ai/acre)	PHI (days)	combined bifenazate/D3598 (ppm)[1]
Dundee, NY (Region 1)	0.51	14	0.27, 0.34
		22	0.13, 0.21
		14	0.10, 0.11
		22	0.08, 0.07
Fresno, CA (Region 10)	0.50	14	0.10, 0.10
		21	0.11, 0.08
Kerman, CA (Region 10)	0.51	14	0.05, 0.09
		21	0.07, 0.04
Tulare, CA (Region 10)	0.52	14	0.05, 0.04
		21	0.01, 0.02
Suisun, CA (Region 10)	0.50	14	0.40, 0.26
		21	0.15, 0.18
Ripon, CA (Region 10)	0.50	14	0.23, 0.17
		21	0.07, 0.06
Upper Lake, CA (Region 10)	0.52	14	0.17, 0.24
		21	0.23, 0.15
Linden, CA (Region 10)	0.55	14	0.19, 0.14
		21	0.11, 0.16
Hughson, CA (Region 10)	0.50	14	0.48, 0.62 HAFT = 0.55
		21	0.50, 0.45
Granger, WA (Region 11)	0.49	14	0.15, 0.19
		21	0.16, 0.13
George, WA (Region 11)	0.50	14	0.28, 0.30
		21	0.18, 0.24

[1] combined bifenazate/D3598 residues expressed as bifenazate

Conclusion: The petitioner submitted grape magnitude of the residue data conducted in Region 1 (n=1), Region 10 (n=8), and Region 11 (n=2). A single application of a 50WP formulation of bifenazate was applied to grapes at 1x the maximum proposed seasonal application rate. The grapes were harvested 14 and 21 days after application and the combined residues of bifenazate/D3598 ranged from 0.04 - 0.62 ppm and 0.01 - 0.50 ppm, respectively (14-day PHI requested). In general, residues decreased as the PHI increased from 14 to 21 days.

Table 5 of OPPTS GLN 860.1500 suggests the following geographical field trial distribution when requesting a tolerance in/on grapes: Region 1 (n=2), Region 10 (n=8), and Region 11 (n=2). An additional field trial conducted in Region 1 is needed to fulfill the suggested geographical distribution. Provided the petitioner agrees to submit the requested field trial data, HED concludes that the available data support the petitioner proposed tolerance of 0.75 ppm for the combined residue of bifenazate and D3598 (expressed as bifenazate) in/on grape.

Hops

MRID 48052323 - UCC-D2341 50WP on Hops: Magnitude of the Residue Study: The in-life phase of the study was conducted by Ron Britt & Associates (Yakima, WA) and Ag Solutions, Inc. (Corvallis, OR) and the analytical portion of the study was conducted by Ricera, Inc. (Painseville, OH). A total of 3 test sites were established during 1999 in Granger, WA (Region 11); Harrah, WA (Region 11); and Mt. Angel, OR (Region 12). Each site consisted of a treated and a control plot. The treated plots received a single application of a 50WP formulation of bifenazate at ~0.75 lbs ai/acre (1x proposed seasonal rate). Applications were made with airblast equipment with spray volumes of ~50 gallons/acre. Single control and triplicate treated samples were collected by hand at maturity 13 or 14 days after treatment. Following sampling, the hops were placed in a commercial hop dryer for 20-24 hours. After drying, the samples were placed in frozen storage within 1 hour and were shipped frozen to the analytical laboratory for analysis. The analytical method was the same as the proposed enforcement method and has been adequately validated (LOQ = 0.05 ppm). The combined residues of bifenazate/D3598 were <0.05 ppm in/on all control samples. The samples were stored for a maximum of 157 days from harvest to analysis (within 7 days of homogenization; no storage stability data is available for hops). Table 22 summarizes the residues of bifenazate/D3598 in/on treated dried hops.

Table 22: Residues of bifenazate/D3598 in/on the Treated Dried Hop Samples

site	treatment rate (lbs ai/acre)	PHI (days)	combined bifenazate/D3598 (ppm)[1]
Granger, WA (Region 11)	0.75	13	8.15, 8.62, 11.15
Harrah, WA (Region 11)	0.75	14	6.28, 8.42, 8.67
Mt. Angel, OR (Region 12)	0.75	14	5.26, 9.85, 6.20

[1] combined bifenazate/D3598 residues expressed as bifenazate

Conclusion: The petitioner submitted hop magnitude of the residue data conducted in Region 11 (n=2) and Region 12 (n=1). A single application of a 50WP formulation of bifenazate was applied to hops at 1x the maximum proposed seasonal application rate. The hops were harvested 14 days after application and dried. The combined residues of bifenazate/D3598 ranged from 5.26 - 11.15 ppm.

Table 1 of OPPTS GLN 860.1500 indicates that a minimum of 3 field trials are required for the establishment of a tolerance in/on hops (geographical distribution is not indicated). Table 6 of OPPTS GLN 860.1500 indicated that 94% of the US crop production of hops comes from Region 11. Therefore, the geographical distribution of the hop field trial data is appropriate. Provided the petitioner can validate the 157 day storage interval (7-day interval from homogenization to analysis should also be validated), the submitted field trial data is appropriate and support the petitioner proposed tolerance of 15 ppm for the combined residues of bifenazate and D3598 (expressed as bifenazate) in/on dried hops. However, the preferred commodity term is "hop, dried cone." The petitioner should submit a revised Section F.

Strawberry

MRID 45076505 - UCC-D2341 50WP on Strawberries: Magnitude of the Residue Study: The in-life phase of the study was conducted by several companies and the analytical portion of the study was conducted by Uniroyal Chemical Co. (Guelph, Ontario). A total of 8 test sites were established during 1999 in New Tripoli, PA (Region 1); Cochran, GA (Region 2); Stanford, FL (Region 3); Noblesville, IN (Region 5); Watsonville, CA (Region 10); Salinas, CA (Region 10); Oceanside, CA (Region 10); and Canby, OR (Region 12). Each site consisted of a treated and a control plot. The treated plots received two foliar applications of a 50WP formulation of bifenazate at ~0.50 lbs ai/acre (1x proposed single application rate). The retreatment interval was 21 days for annual plants (single harvest) and 45 days for ever-bearing plants (multi-harvest). Applications were made with broadcast spray equipment with spray volumes of ~100 gallons/acre. Single control and duplicate treated samples were collected by hand at maturity 1 and 3 days after the second treatment. The harvested strawberries were placed in a freezer within 4 hours of collection and were shipped frozen to the analytical laboratory for analysis. The analytical method was the same as the proposed enforcement method. Validation of the method for determination of bifenazate in/on strawberries was performed and resulted in adequate recoveries. Validation of the method for determination of D3598 in/on strawberries was not performed in conjunction with this study. However, the method has been previously validated for determination of D3598 in/on apple, pear, peach, grape, plum and oranges and is therefore considered to be adequately validated for the purposes of this study (LOQ = 0.01 ppm). The combined residues of bifenazate/D3598 were <0.01 ppm in/on all control samples. The samples were stored for a maximum of 175 days from harvest to analysis (analyzed within 5 days of homogenization). No strawberry storage stability data has been submitted validating this interval (see OPPTS GLN 860.1380 Storage Stability Section). Table 23 summarizes the residues of bifenazate/D3598 in/on treated strawberry.

Table 23: Residues of Bifenazate/D3598 in/on the Treated Strawberries

site	treatment rates (lbs ai/acre) and retreatment interval	PHI (days)	combined bifenazate/D3598 (ppm)[1]
New Tripoli, PA (Region 1)	0.50, 0.50 21 days	1	0.63, 0.72
		3	0.45, 0.41
Cochran, GA (Region 2)	0.50, 0.49 21 days	1	0.93, 0.93
		3	0.81, 0.80
Sanford, FL (Region 3)	0.50, 0.54 21 days	1	0.45, 0.43
		3	0.40, 0.47
Nobelsville, IN (Region 5)	0.50, 0.50 21 days	1	1.1, 0.93
		3	0.40, 0.42
Watsonville, CA (Region 10)	0.48, 0.48 45 days	1	0.60, 0.65
		3	0.62, 0.61
Salinas, CA (Region 10)	0.50, 0.49 45 days	1	0.21, 0.24
		3	0.27, 0.31
Oceanside, CA (Region 10)	0.51, 0.50 45 days	1	0.42, 0.45
		3	3.4, 2.9
Canby, OR (Region 12)	0.50, 0.50 21 days	1	0.56, 0.50
		3	0.23, 0.25

[1] combined bifenazate/D3598 residues expressed as bifenazate

Conclusion: The petitioner submitted strawberry magnitude of the residue data conducted in Region 1 (n=1), Region 2 (n=1), Region 3 (n=1), Region 5 (n=1), Region 10 (n=3), and Region 12 (n=1). The strawberry plants were treated twice with a 50WP formulation of bifenazate at 1x the maximum proposed single application rate (retreatment interval of 21 or 45 days). The proposed label states that 2 applications are permitted per year with only a single application per harvested crop (retreatment interval of 21 days). Using this treatment scenario, it is likely that early fruiting strawberries may be exposed to two applications of bifenazate and the treatment scenario employed is appropriate for determination of maximum residues. The strawberries were harvested 1 day and 3 days after the second application and the combined residues of bifenazate/D3598 ranged from 0.21 - 1.1 ppm and 0.23 - 3.4 ppm, respectively (1-day PHI requested). The samples harvested 3 days after application from Oceanside, CA resulted in combined bifenazate/D3598 residues of 2.9 and 3.4 ppm. These concentrations are most likely a result of analytical error for the following reasons: **(1)** these values are at least 5x greater then the residues found on the remaining samples harvested 3 days after application, **(2)** the sample collected 1 day after application from this site had a combined bifenazate/D3598 residues of 0.42 ppm and 0.45 ppm, and **(3)** the other sites generally showed a reduction in residues as the pre-harvest interval increased from 1 to 3. Consequently, the samples harvested 3 days after application from Oceanside, CA will not be used when determining the appropriate tolerance. When excluding the Oceanside, CA data the combined residues of bifenazate/D3598 for samples harvested 3 days after application ranged from 0.23 - 0.81 ppm.

Table 5 of OPPTS GLN 860.1500 suggests the following geographical field trial distribution when requesting a tolerance in/on strawberries: Region 1 (n=1), Region 2 (n=1), Region 3 (n=1), Region 5 (n=1), Region 10 (n=3), and Region 11 (n=1). The geographical distribution of the strawberry field trial data is sufficient for registration. Provided the petitioner can validate the 175-day storage interval (5-day interval from homogenization to analysis should also be validated), HED concludes that the available data support the petitioner proposed tolerance of 1.5 ppm for the combined residues of bifenazate and D3598 (expressed as bifenazate) in/on strawberries.

Cotton

MRID 45052327 - UCC-D2341 50WP on Cotton: Magnitude of the Residue and Processing Study: The in-life phase of the study was conducted by several companies and the analytical portion of the study was conducted by Ricerca, Inc. (Painsesville, OH). A total of 11 test sites were established during 1999 in Elko, SC (Region 2); Senatobia, MS (Region 4); Rosa, LA (Region 4); Cheneyville, LA (Region 4); Colony, OK (Region 6); Levelland, TX (Region 8); Vernon, TX (Region 8); Edmonson, TX (Region 8); Rincom, NM (Region 8); Hickamn, CA (Region 10); and Madera, CA (Region 10). Each site consisted of a treated and a control plot. The treated plots received a single application of a 50WP formulation of bifenazate at ~0.75 lbs ai/acre (1x proposed seasonal application rate). Applications were made with broadcast spray equipment with spray volumes of ~20 gallons/acre. The cotton was harvested at maturity ~60 days after application (42 days at one of the sites) using mechanical spindle or stripper pickers or by hand. The harvested cotton was either ginned near the field site on the same day as harvest (after the sample was ginned it was placed in frozen storage) or was held at ambient temperatures and shipped to Texas A & M Food Protein R & D Center (Bryan, TX) and ginned (samples shipped within 2 days of harvest; once at the processing facility the samples were stored frozen). Once the cottonseed and cotton gin byproduct sample had been collected they were sent to the analytical laboratory for analysis. The analytical method was the same as the proposed enforcement method and has been adequately validated (LOQ = 0.01 ppm). The combined residues of bifenazate/D3598 were <0.01 ppm in/on all cottonseed control samples and in/on 6 of the 9 cotton gin byproduct control samples (0.37, 0.08, and 0.02 ppm). The cottonseed and cotton gin byproduct samples were stored frozen for a maximum of 56 and 42 days, respectively, from harvest to analysis. The storage stability data indicate that residues of bifenazate and D3598 were not stable in/on

cottonseed when stored frozen for 21 days (the shortest interval tested) or in/on cotton gin byproduct when stored frozen for 44 days (the shortest interval tested). Since the samples were being harvested on different days and some of the samples had to be sent to a processor to be ginned using commercially simulated practices, HED concludes that the interval from harvest to analysis was reasonable and will not invalidate the data due to the lack of stability of bifenazate and D3598. However, a correction factor of 0.57 and 0.60 will be applied to the cottonseed and cotton gin byproduct residue data. The correction factors were based on the average recoveries of bifenazate and D3598 in/on from the storage stability data. Table 24 summarizes the residues of bifenazate/D3598 in/on cottonseed and cotton gin byproduct samples.

Table 24: Residues of Bifenazate/D3598 in/on the Treated Cottonseed and Cotton Gin Byproduct

site	treatment rate (lbs ai/acre)	PHI (days)	harvesting equipment	ginning location	storage interval (days)[1]	combined bifenazate/ D3598 (ppm)[2]	corrected bifenazate/ D3598 (ppm)[3]
cottonseed							
Elko, SC (Region 2)	0.76	61	spindle	processor	56	<0.01, <0.01	<0.02, <0.02
Senatobia, MS (Region 4)	0.73	59	hand	field	19	<0.01, <0.01	<0.02, <0.02
Rosa, LA (Region 4)	0.75	60	spindle	field	8	<0.01, <0.01	<0.02, <0.02
Cheneyville, LA (Region 4)	0.76	60	spindle	processor	15	<0.01, <0.01	<0.02, <0.02
Colony, OK (Region 6)	0.75	60	hand	field	35	<0.01, <0.01	<0.02, <0.02
Levelland, TX (Region 8)	0.76	59	stripper	processor	43	<0.01, <0.01	<0.02, <0.02
Vernon, TX (Region 8)	0.75	42	stripper	processor	26	0.02, 0.02	0.04, 0.04
Edmonson, TX (Region 8)	0.75	59	stripper	processor	36	0.01, 0.01	0.02, 0.02
Rincom, NM (Region 8)	0.75	60	spindle	processor	32	0.07, 0.05	0.12, 0.09
Hickman, CA (Region 10)	0.73	61	hand	field	29	<0.01, <0.01	<0.02, <0.02
Madera, CA (Region 10)	0.76 0.74	60 61	spindle spindle	field processor	20 50	0.06, 0.01 0.31, 0.25	0.11, 0.02 0.54, 0.44 **HAFT = 0.49**
cotton gin byproducts							
Elko, SC (Region 2)	0.76	61	spindle	processor	34	0.91, 0.84	1.52, 1.40
Cheneyville, LA (Region 4)	0.76	60	spindle	processor	31	1.42, 1.22	2.37, 2.03
Levelland, TX (Region 8)	0.76	59	stripper	processor	37	0.07, 0.06	0.12, 0.10
Vernon, TX (Region 8)	0.75	42	stripper	processor	23	0.43, 0.49	0.72, 0.82
Edmonson, TX (Region 8)	0.75	59	stripper	processor	35	0.38, 0.40	0.63, 0.67
Rincom, NM (Region 8)	0.75	60	spindle	processor	30	4.02, 4.03	6.70, 6.72
Madera, CA (Region 10)	0.74	61	spindle	processor	42	17.5, 18.4	29.17, 11.04

[1] storage interval from harvest to analysis

[2] combined bifenazate/D3598 residues expressed as bifenazate

[3] corrected for average % recovery of bifenazate and D3598 from storage stability study; 0.57 for cottonseed (stored for 56 days) and 0.60 for cotton gin byproduct (stored for 44 days)

Conclusion: The petitioner submitted cottonseed magnitude of the residue data conducted in Region 2 (n=1), Region 4 (n=3), Region 6 (n=1), Region 8 (n=4), and Region 10 (n=2). A single application of a 50WP formulation of bifenazate was applied to cotton at 1x the maximum proposed seasonal application rate. The cotton was harvested by hand or with mechanical spindle or stripper pickers 60 days after application. The harvested cotton was ginned either at the field site or buy a processor into undelinted cottonseed which was subsequently analyzed. The combined residues of bifenazate/D3598 ranged from <0.02 - 0.54 ppm (residues corrected for loss due to lack of stability; see OPPTS GLN 860.1380 Storage Stability section).

Table 5 of OPPTS GLN 860.1500 suggests the following geographical distribution when submitting cottonseed residue data: Region 2 (n=1), Region 4 (n=3), Region 6 (n=1), Region 8 (n=4), and Region 10 (n=3). An additional field trial conducted in Region 10 is needed to fulfill the suggested geographical distribution. Provided the petitioner agrees to submit the requested field trial data, HED concludes that the available data support a tolerance of 0.75 ppm for the combined residues of bifenazate and D3598 (expressed as bifenazate) in/on cottonseed. However, the correct commodity definition is "cotton, undelinted seed." A revised Section F should be submitted.

The petitioner submitted cotton gin byproduct magnitude of the residue data conducted in Region 2 (n=1), Region 4 (n=1), Region 8 (n=4), and Region 10 (n=1). A single application of a 50WP formulation of bifenazate was applied to cotton at 1x the maximum proposed seasonal application rate. The cotton was harvested with a mechanical spindle (n=4) or stripper (n=3) pickers 60 days after application. The harvested cotton was ginned by a processor into cotton gin byproduct which was subsequently analyzed. The combined residues of bifenazate/D3598 ranged from 0.10 - 29.17 ppm (residues corrected for loss due to lack of stability; see OPPTS GLN 860.1380 Storage Stability section)

Table 1 of OPPTS 860.1000 indicates that the petitioner should submit cotton gin byproduct data from a minimum of 6 field trials (3 samples harvested using a stripper and 3 samples harvested using a mechanical picker). The submitted cotton gin byproduct data fulfills the data requirements for cotton gin byproduct. HED concludes that the available data support a tolerance of 35 ppm for the combined residues of bifenazate and D3598 (expressed as bifenazate) in/on cotton, gin byproducts. A revised Section F should be submitted.

OPPTS GLN 860.1520: Processed Food/Feed

Cotton

MRID 45052327 - UCC-D2341 50WP on Cotton: Magnitude of the Residue and Processing Study: The in-life phase of the study was conducted by Marathon Agricultue (Las Cruces, NM) and ABC Laboratories (Madera, CA) and the analytical portion of the study was conducted by Ricerca, Inc. (Painsesville, OH). Test sites were established during 1999 in Rincom, NM (Region 8) and Madera, CA (n=2, Region 10). Each site consisted of a treated and a control plot. The treated plots received a single application of a 50WP formulation of bifenazate at ~4.73 lbs ai/acre (6.3x proposed seasonal application rate). Applications were made with broadcast spray equipment with spray volumes of ~20 gallons/acre. The cotton was harvested at maturity ~60 days after application using a spindle picker. The harvested cotton was held at ambient temperatures and shipped to Texas A & M Food Protein R & D Center (Bryan, TX) to be processed into cottonseed, hulls, meal and oil (samples shipped within 2 days of harvest; once at the processing facility the samples were stored frozen). The cotton was processed using simulated commercial practices and sent to the analytical laboratory for analysis (processing initiated within 20 days of harvest). The analytical method was the same as the proposed enforcement method and has been adequately validated (LOQ = 0.01 ppm). The combined residues of bifenazate/D3598 were <0.01 ppm in/on all control samples. The cottonseed, hull, meal, and oil

samples were analyzed 50, 47, 39, and 48 days after collection (hulls, meal, and oil were analyzed 70, 63, and 73 days after cotton harvest). The storage stability data submitted in conjunction with this study indicate that residues of bifenazate and D3598 were not stable in/on cottonseed (21 days was the shortest interval tested) or in/on cottonseed meal (43 days was the shortest interval tested) and were stable in/on hulls and oil for 52 days and 28 days, respectively (longest interval tested). Since the samples were being harvested on different days and coordination with the processor and analytical laboratory where required, HED concludes that the interval from harvest or collection to analysis (maximum of 50 days) was reasonable and will not invalidate the data due to the instability of bifenazate and D3598. However, a correction factor of 0.57 and 0.70 will be applied to the cottonseed and cottonseed meal residue data. The correction factors were based on the average recoveries of bifenazate and D3598from the storage stability data. Table 25 summarizes the residues of bifenazate/D3598 in/on treated cottonseed and cottonseed processed commodities.

Table 25: Residues of Bifenazate/D3598 in/on Cottonseed and Cottonseed Processed Commodities

	matrix	combined bifenazate/D3598 (ppm)[1]	corrected bifenazate/D3598 (ppm)[2]	concentration factor[3]
Rincon, NM (Region 8)	cottonseed	1.24, 0.85; avg = 1.05	1.88	na
	hulls	0.13, 0.09; avg = 0.11	0.11	0.1
	meal	<0.01, <0.01	<0.01	<0.01
	refined oil	<0.01, <0.01	<0.01	<0.01
Madera, CA (Region 10)	cottonseed	2.72, 2.55; avg = 2.64	4.63	na
	hulls	0.88, 0.95; avg = 0.92	0.92	0.2
	meal	<0.01, <0.01	<0.01	<0.01
	refined oil	<0.01, <0.01	<0.01	<0.01

[1] combined bifenazate/D3598 residues expressed as bifenazate

[2] corrected for average % recovery of bifenazate and D3598 from storage stability study; 0.57 for cottonseed (stored for 56 days) and 0.70 for cottonseed meal (stored for 43 days); storage interval for hulls and oil were validated by the storage stabiity data (no correction applied)

[3] concentration factor = average concentration in processed commodity divide by average concentration in RAC

Conclusion: A single application of a 50WP formulation of bifenazate was applied to cotton at 6x the maximum proposed seasonal application rate. The cotton was harvested 60 days after application and processed into seed, hulls, meal, and refined oil. The resulting data indicate that the combined residues of bifenazate/D3598 reduced as the cottonseed was processed into hulls (0.2x), meal (<0.01x), and refined oil (<0.01x). Therefore, tolerances for the processed commodities will be covered by the RAC.

Plum

MRID 45052326 - UCC-D2341 50WP on Stonefruit: Magnitude of the Residue and Processing Study: The in-life phase of the study was conducted by Hulst Res. Services, Inc. (Fresno, CA) and Ag Solutions (Corvallis, OR) and the analytical portion of the study was conducted by Ricerca, Inc. (Paineseville, OH). Plum test sites were established during 1998 in Davis, CA (Region 10) and Dallas, OR (Region 12). Each site consisted of a treated and a control plot. The treated plots received a single application of a 50WP formulation of bifenazate at ~0.50 lbs ai/acre (1x proposed seasonal application rate). Applications were made with airblast equipment with spray volumes of ~50 gallons/acre. Single control and duplicate treated samples were collected by hand at maturity 3 days after treatment and were shipped at ambient temperatures within 1 day to Hulst Res. Services, Inc. (Fresno, CA) for processing. Once at the processing facility the plums were washed and placed in a drying tunnel for 18-27 hours (samples were processed within 1 day of arrival). After drying, the samples were placed in frozen storage and shipped to the analytical laboratory along with the frozen RAC for analysis. The analytical method was the same as the proposed enforcement method and has been adequately validated (LOQ = 0.01 ppm). The plums and prunes were analyzed within 21 days of harvest (within 6 days of homogenization; adequate storage stability data validates this interval). The combined residues of bifenazate/D3598 were <0.01 ppm in/on all of the control samples. Table 26 summarizes the residues of bifenazate/D3598 in/on treated plum and prune.

Table 26: Residues of Bifenazate/D3598 in/on Plum and Prune

	matrix	combined bifenazate/D3598 (ppm)[1]	concentration factor[2]
Davis, CA (Region 10)	plum	0.02, 0.02; avg = 0.02	na
	prune	0.01, 0.01; avg = 0.01	0.5
Dallas, OR (Region 12)	plum	0.03, 0.03; avg = 0.03	na
	prune	<0.01, <0.01	<0.33

[1] combined bifenazate/D3598 residues expressed as bifenazate

[2] concentration factor = average concentration in processed commodity divide by average concentration in RAC

Conclusion: A single application of a 50WP formulation of bifenazate was applied to plum trees at 1x the maximum proposed seasonal application rate. Plums were harvested 3 days after application and processed into prunes. The resulting data indicated that the combined residues of bifenazate/D3598 reduced as the plums were processed to prunes (0.5x). Therefore, tolerances for the processed commodities will be covered by the RAC.

Apple

MRID 45052324 - UCC-D2341 50WP on Apples: Processing Study: The in-life phase of the study was conducted by A.C.D.S. Research, Inc. (Williamson, NY) and Ron Britt & Associates (Yakima, WA) and the analytical portion of the study was conducted by Uniroyal Chemical Co. (Guelph, Ontario). Test sites were established during 1998 in North Rose, NY (Region 1) and Zillah, WA (Region 11). Each site consisted of a treated and a control plot. The treated plots received a single application of a 50WP formulation of bifenazate at ~2.5 lbs ai/acre (5x proposed seasonal application rate). Applications were made with airblast equipment with spray volumes of ~50 gallons/acre. Single control and duplicate treated samples were collected by hand at maturity 7 days after treatment and

were shipped at ambient temperatures on the day of harvest to A.C.D.S. Research, Inc. (North Rose, NY) for processing. Once at the processing facility, the apples were stored in a cooler and were processed into juice and pomace within 2 days of harvest. The processed commodities were placed in frozen storage upon collection and shipped to the analytical laboratory along with the frozen RAC for analysis. The analytical method was the same as the proposed enforcement method. Validation data for bifenazate was presented and resulted in adequate recoveries. Validation of the method for determination of D3598 in/on apple, apple juice, and apple pomace was not performed. However, the method has been previously validated for determination of D3598 in/on apples and is therefore considered to be adequately validated for the purposes of this study (LOQ = 0.01 ppm). Whole apples, apple juice, and wet apple pomace were analyzed within 251 (within 4 days of homogenization), 295, and 295 days, respectively. The petitioner has submitted adequate data validating the storage interval for whole apples. No storage stability data for apple juice and wet apple pomace have been submitted (grape juice stability data has been submitted but this only validates a 186 day storage interval). The combined residues of bifenazate/D3598 were <0.01 ppm in/on all of the control samples. Table 27 summarizes the residues of bifenazate/D3598 in/on treated apple, apple juice, and wet apple pomace.

Table 27: Residues of Bifenazate/D3598 in/on Whole Apple, Apple Juice, and Wet Apple Pomace

	matrix	combined bifenazate/D3598 (ppm)[1]	concentration factor[2]
North Rose, NY (Region 1)	whole apple	0.89, 0.88; avg = 0.88	--
	apple juice	0.24, 0.16; avg = 0.20	0.23
	wet apple pomace	1.7, 1.5; avg = 1.6	1.82
Zillah, WA (Region 11)	whole apple	1.9, 2.2; avg = 2.0	--
	apple juice	0.19, 0.24; avg = 0.22	0.11
	wet apple pomace	3.5, 3.6; avg = 3.6	1.80

[1] combined bifenazate/D3598 residues expressed as bifenazate

[2] concentration factor = average concentration in processed commodity divide by average concentration in RAC

Conclusion: A single application of a 50WP formulation of bifenazate was applied to apple trees at 5x the maximum proposed seasonal application rate. Apples were harvested 7 days after application and processed into juice and wet pomace. The resulting data indicate that the combined residues of bifenazate/D3598 reduced in apple juice (0.23x) but concentrated in wet apple pomace (1.82x). The HAFT for apples was 0.58 ppm. Provided the petitioner can validate the 295-day storage interval for apple juice and wet apple pomace, HED concludes that an apple juice tolerance is unnecessary and the petitioner proposed tolerance for the combined residues of bifenazate and D3598 (expressed as bifenazate) in/on wet apple pomace of 1.2 ppm is appropriate (HAFT x processing factor = 0.58 x 1.82 = 1.1 ppm). However, the preferred commodity term is "apple, wet pomace." A revised Section F should be submitted.

Grape

MRID 45052325 - UCC-D2341 50WP on Grapes: Processing and Decline Study: The in-life phase of the study was conducted by California Agricultural Research, Inc. (Kerman, CA) and TRACS, Inc. (Visalia, CA) and the analytical portion of the study was conducted by Ricerca, Inc. (Painesville, OH). Test sites were established during 1998 in Kerman, CA (Region 10) and Dinuba, CA (Region 10). Each site consisted of a treated and a control plot. The treated plots received a single application of a 50WP formulation of bifenazate at ~2.5 lbs ai/acre (5x proposed seasonal application rate). Applications were made with airblast equipment with spray volumes of ~50 gallons/acre. Single control and duplicate treated samples were collected by hand at maturity 14 days after treatment and shipped at ambient temperature within 1 day of harvest to Englar Food Laboratories, Inc. (Moses Lake, WA) for processing into grape juice. Once at the processing facility, the grapes were stored in a cooler and were processed into juice within 3 days of harvest. The juice sample was placed in frozen storage and shipped along with the frozen RAC to the analytical laboratory for analysis. Grape samples collected for processing into raisins were harvest 14 days after application and were allowed to dry under field conditions for 14-15 days. The raisin samples were collected, placed in frozen storage, and shipped along with the frozen RAC sample to the analytical laboratory. The analytical method was the same as the proposed enforcement method and has been adequately validated (LOQ = 0.01 ppm). Grape, grape juice, and raisin samples were analyzed within 12 (within 1 day of homogenization), 15, and 26 (within 7 days of homogenization) days, respectively, of harvest. The petitioner has submitted adequate data validating these storage intervals. The combined residues of bifenazate/D3598 were <0.01 ppm in/on all of the control samples. Table 28 summarizes the residues of bifenazate/D3598 in/on treated grape, grape juice, and raisin.

Table 28: Residues of Bifenazate/D3598 in/on Grape, Grape Juice, and Raisin

	matrix	combined bifenazate/D3598 (ppm)[1]	concentration factor[2]
Kerman, CA (Region 10)	grape	0.31, 0.24; avg = 0.28	--
	grape juice	0.02, 0.01; avg = 0.02	0.07
	grape	0.30, 0.29; avg = 0.30	--
	raisin	0.07, 0.13; avg = 0.10	0.33
Dinuba, CA (Region 10)	grape	0.14, 0.09; avg = 0.12	--
	grape juice	0.02, 0.02; avg = 0.02	0.17
	grape	0.15, 0.22; avg = 0.18	--
	raisin	0.40, 0.34; avg = 0.37	2.06

[1] combined bifenazate/D3598 residues expressed as bifenazate

[2] concentration factor = average concentration in processed commodity divide by average concentration in RAC

Conclusion: A single application of a 50WP formulation of bifenazate was applied to grape vines at 5x the maximum proposed seasonal application rate. Grapes were harvested 14 days after application and processed into juice and raisins and the samples were analyzed for bifenazate/D3598. The resulting data indicate that the combined residues of bifenazate/D3598 reduced in grape juice (0.17x) but concentrated in raisin (2.06x). The HAFT for grapes was 0.55 ppm. HED concludes that a grape juice tolerance is unnecessary and a tolerance for the combined residues of bifenazate and D3598 (expressed as bifenazate) in/on raisin of 1.2 ppm is appropriate (HAFT x processing factor = 0.55 x 2.06 = 1.1). The preferred commodity term is "grape, raisin." A revised Section F should be submitted.

OPPTS GLN 860.1850: Confined Accumulation in Rotational Crops

MRID 45052328 - A Confined Rotational Crop Study with [^{14}C]D2341: The in-life and analytical phases of the study were conducted by Ricerca Inc. (Painesville, OH). [^{14}C]Bifenazate (246,154 dpm/µg; ≥98% radiochemical purity; substituted phenyl ring labeled) was mixed with unlabeled bifenazate (final activity of 70,000 dpm/µg), added to a formulation blank, mixed with water, and applied to soil in pots at a rate equivalent to 0.5 lbs ai/acre (0.7x the maximum single and seasonal application rate for crops likely to be rotated). A second application solution was prepeared (20,000 dpm/µg) and applied to soil in pots at a rate equivalent to 5.0 lbs ai/acre (6.7x the maximum single and seasonal application rate for crops likely to be rotated). The soil was aged for 30, 125, and 365 days and was planted with carrot, lettuce, and wheat (soil aged for 365 days was only planted with wheat). Immature and/or mature samples were collected from all time intervals and application rates, homogenized, and stored frozen. TRR are summarized in Table 29.

Table 29: TRR in Rotated Crops

	plant back interval (days)	TRR	
		0.5 lbs ai/acre	5.0 lbs ai/acre
immature lettuce	30	0.015	0.146
	125	0.013	0.086
mature lettuce	30	0.014	0.080
	125	0.005	0.039
immature carrot	30	0.033	0.270
	125	0.010	0.078
mature carrot	30	0.007	0.095
	125	0.006	0.042
wheat forage	30	0.038	0.382
	125	0.020	0.164
	360	0.018	not planted
wheat hay	30	0.117	0.748
	125	0.051	0.257
	360	0.033	not planted
wheat chaff	30	0.031	0.226
	125	0.025	0.162
	360	0.015	not planted
wheat grain	30	0.016	0.178
	125	0.019	0.122
	360	0.011	not planted

Extraction and Characterization of Residues: The 30-day immature lettuce, 30-day mature lettuce, 30-day immature carrot, and the 30- and 125-day wheat forage, hay, chaff, and grain from the 0.5 lbs ai/acre samples were extracted as follows. The homogenized samples were extracted with ACN followed by ACN/water. The PES of lettuce, carrot, wheat forage, wheat chaff, and wheat grain were not further analyzed (TRR <0.05 ppm). The PES of wheat hay were >0.05 ppm. To attain greater residues the 30-day wheat hay sample from the 5.0 lbs ai/acre treatment was extracted and subsamples of the PES were hydrolyzed with mild acid (1N HCl), mild base (1N NaOH), cellulase followed by hemicellulase, and strong acid (72% sulfuric acid).

Instrumental Analysis: Only samples planted into soil treated at 0.5 lbs ai/acre were discussed. The ACN and ACN/water extractable residues were >0.01 ppm for only 30-day wheat forage and the 30- and 125-day wheat hay. These samples, together with the 30-day ACN extracts of immature lettuce, mature lettuce, and immature carrot, were HPLC analyzed. Residues were identified by cochromatography with the following standards: bifenazate, D3598, D1989, D4111, D5863, D6887, D4642, A1530, D9472, and D9477. The HPLC effluent was monitored by a in-line radioactivity flow detector and quantitation was by fraction collection followed by LSC analysis (LOQ = 0.003 ppm). No analytes were identified.

The chromatograms of the soluble fractions showed two broad unresolved areas (2-4 minute region; 18-37 minute region). TRR in these regions were <0.01 ppm for all samples except for the 18-37 minute region of the 30-wheat straw sample (0.022 ppm). To better characterize this region, the 30-day wheat straw sample from the 5.0 lbs ai/acre treatment was extract with ACN and ACN/water and the 18-37 minute region was isolated. The isolated region was hydrolyzed with β-glucosidase, 2N HCl, and 2N NaOH. Analysis of the β-glucosidase hydrolysate resulted in a chromatographic profile similar to the unhydrolyzed extract. Some change were noted in the acid and base HPLC profiles but none of the resulting peaks could be identified with the available standards (peaks represented ≤0.008 ppm by extrapolation to 0.50 lbs ai/acre rate).

Storage Stability: The petitioner indicated that the samples were stored at <-5 C prior to extraction and were analyzed within 30 days of harvest. A 30-day wheat forage sample was extracted after 3 months of storage and the extracts were HPLC analyzed. The resulting data was compared to the initial analysis and demonstrated that residues of bifenazate were stable in wheat forage. Since the samples were analyzed within 30 days of harvest, the submitted storage stability data is sufficient to validate this study. Table 30 summarizes the residues identification/characterization.

Table 30: Residue Identification and Characterization[1]

	ppm [^{14}C]bifenazate equivalents; %TRR			
	total	**ACN**	**ACN/water**	**PES**
30-day immature lettuce				
total	0.015	0.005; 33%	<0.003; 0%	0.007; 47%
0-7 minute region	0.004; 26%	0.004; 26%	na	na
30-day mature lettuce				
total	0.014	0.004; 29%	<0.003; 0%	0.008; 57%
2-4 minute region	0.001; 6%	0.001; 6%	na	na
20-35 minute region	0.003; 18%	0.003; 18%	na	na

	ppm [^{14}C]bifenazate equivalents; %TRR			
	total	ACN	ACN/water	PES
30-day immature carrot				
total	0.033	0.009; 27%	0.003; 9%	0.016; 48%
3-4 minute region	0.001; 4%	0.001; 4%	na	na
20-35 minute region	0.007; 22%	0.007; 22%	na	na
30-day wheat forage				
total	0.038	0.012; 32%	0.008; 21%	0.017; 45%
3-4 minute region	0.002; 4%	0.001; 2%	0.001; 1%	na
18-37 minute region	0.016; 42%	0.009; 25%	0.007; 18%	na
125-day wheat forage				
total	0.020	0.005; 25%	<0.001; 0%	0.015; 75%
3-4 minute region	0.001; 3%	0.001; 3%	na	na
18-37 minute region	0.003; 17%	0.003; 17%	na	na
30-day wheat straw				
total	0.117	0.013; 11%	0.031; 26%	0.072; 62%
3-4 minute region	0.007; 6%	0.002; 2%	0.005; 4%	--
18-37 minute region	0.029; 24%	0.007; 6%	0.022[2]; 18%	--
procedures performed on PES[3]				
1N HCl				0.005; 7%
1N NaOH				0.040; 36%
cellulase				0.019; 16%
hemicullulase				0.004; 3%
H_2SO_4				0.025; 21%
125-day wheat straw				
total	0.051	0.004; 8%	0.008; 16%	0.036; 71%
3-4 minute region	0.002; 4%	<0.003; 0.4%	0.002; 3%	na
18-37 minute region	0.008; 16%	0.003; 6%	0.005; 10%	na
wheat grain				
30-day	0.016	<0.001; 0.0%	0.004; 25%	0.012; 75%
125-day	0.019	0.002; 10%	0.003; 16%	0.014; 74%
due to the low TRR (<0.01 ppm) in the extracts, no HPLC analysis was performed				
wheat chaff				
30-day	0.031	<0.001; 0.0%	0.004; 13%	0.024; 77%
125-day	0.025	<0.001; 0.0%	0.004; 16%	0.020; 80%
360-day	0.015	<0.001; 0.0%	0.008; 53%	0.008; 53%
due to the low TRR (<0.01 ppm) in the extracts, no HPLC analysis was performed				

na not further analyzed; residue <0.01 ppm for extracts or <0.05 for PES

[1] data from samples grown in soil treated at 0.5 lbs ai/acre

[2] no single one minute fraction contained >0.002 ppm (1.6% TRR)

[3] sub-samples of post extraction solids hydrolyzed as follows

Conclusion: [^{14}C]Bifenazate (substituted phenyl ring labeled) was applied to soil in pots at a rate equivalent to 0.5 lbs ai/acre or 5.0 lbs ai/acre (0.7x and 6.7x the maximum single and seasonal application rate for crops likely to be rotated). The soil was aged for 30, 125, and 365 days and was planted with carrot, lettuce, and wheat (soil aged for 365 days was only planted with wheat). The total radioactive residues (TRR) in 30-day mature lettuce, 30-day mature carrot, and 30-day wheat forage, hay, chaff, and grain samples harvested from the 0.5 lbs ai/acre treated soil were 0.014, 0.007, 0.038, 0.117, 0.031, and 0.016 ppm, respectively.

The 30-day immature lettuce, 30-day mature lettuce, 30-day immature carrot, 30-day wheat grain and chaff, and the 30- and 125-day wheat forage and hay samples were homogenized and extracted with ACN followed by ACN/water. Only the postextraction solids (PES) of wheat hay were >0.05 ppm and were hydrolyzed with mild acid (1N HCl), mild base (1N NaOH), cellulase followed by hemicellulase, and strong acid (72% sulfuric acid; if PES are >0.05 ppm additional characterization is required). The resulting extracts and hydrolysates were HPLC analyzed and the petitioner did not associated any of the radioactivity with available standards. Based on a review of the submitted chromatograms and retention time of the standards, HED concludes the following: **(1)** D9472 may be present in the 30-day mature lettuce and immature carrot ACN extracts (TRR in these extracts were 0.004 and 0.009); **(2)** D9472 and D9569 may be present in the 30-day wheat forage ACN extract (TRR in the extract 0.012 ppm); **(3)** D3598 may be present in the 30-day wheat straw ACN extract (TRR in the extract was 0.013 ppm); and **(4)** D9569 and D9472 may be present in the 30-day wheat forage ACN/water extract (TRR in the extract was 0.008 ppm).

The MARC reviewed the confined rotational crop study and concluded that residues of concern in/on rotational crops could not be determined from the available data (D276801, T. Bloem, 16-Aug-2001). Provided the petitioner includes a 30-day rotational crop restriction for all non-labeled crops (a revised Section B should be submitted), HED concludes that tolerances for rotational crops are not necessary for the following reasons: **(1)** TRR in mature carrot planted 30 days after treatment were <0.01 ppm (0.007 ppm); **(2)** TRR in mature lettuce planted 30 days after treatment were 0.014 ppm. However upon analysis no residue >0.01 ppm could be identified; and **(3)** TRR in and 30-day wheat forage, wheat hay, wheat chaff, and wheat grain were 0.038 ppm, 0.117 ppm, 0.031 ppm, and 0.016 ppm, respectively. However, upon analysis no residues >0.01 ppm could be identified.

attachment 1: international residue limit status sheet
attachment 2: chemical structures
attachment 3: petitioner proposed metabolic pathway in apple
attachment 4: petitioner proposed metabolic pathway in citrus
attachment 5: petitioner proposed metabolic pathway in cotton
attachment 6: petitioner proposed metabolic pathway in ruminant
attachment 7: petitioner proposed metabolic pathway in poultry

cc: PP# 7F04923, T. Bloem (RAB1)
RDI: RAB1 Chemist (16-Aug-2001); ChemSAC (22-Aug-2001)
T. Bloem:806R:CM#2:(703)605-0217:7590C

attachment 1: IRLS sheet

INTERNATIONAL RESIDUE LIMIT STATUS

Chemical Name: hydrazine carboxylic acid, 2-(4-methoxy-[1,1'-biphenyl]-3-yl)-,1-methylethyl ester	Common Name: bifenazate	x□ Proposed tolerance □ Reevaluated tolerance □ Other	Date: 12/21/2000

Codex Status (Maximum Residue Limits)	U. S. Tolerances
X No Codex proposal step 6 or above □ No Codex proposal step 6 or above for the crops requested	Petition Number: 0F06108 DP Barcode: Other Identifier:
Residue definition (step 8/CXL): N/A	Reviewer/Branch:Tom Bloem/RAB1
	Residue definition: **plants** - bifenazate and diazenecarboxylic acid, 2-(4-methoxy-[1,1'-biphenyl]-3-yl)-,1-methylethyl ester **livestock** - bifenazate, diazenecarboxylic acid, 2-(4-methoxy-[1,1'-biphenyl]-3-yl)-,1-methylethyl ester, (1,1'-biphenyl)-4-ol, and (1,1'-biphenyl)-4-hydrogensulfate, sodium salt * = cattle, goats, horses, hogs, and sheep

Crop (s)	MRL (mg/kg)	Crop(s)	Tolerance (ppm)
		cottonseed	0.5
		cotton gin by products	20
		grapes	0.75
		hops	15
		*meat	0.02
		milk	0.01
		pome fruit	0.75
		wet apple pomace	1.2
		stone fruit	1.5
		strawberries	1.5

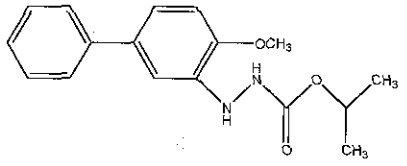
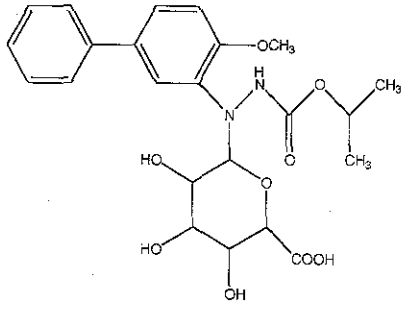
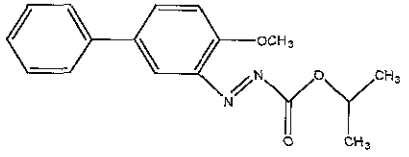
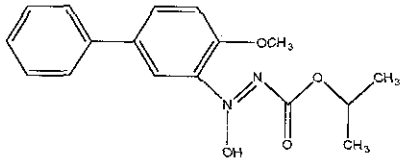
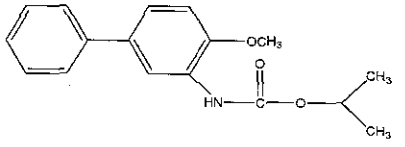
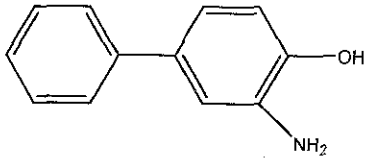
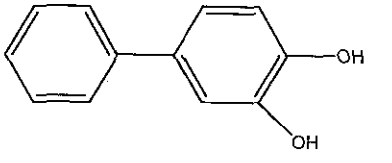
Limits for Canada	Limits for Mexico
X No Limits □ No Limits for the crops requested	X No Limits □ No Limits for the crops requested
Residue definition: N/A	Residue definition: N/A

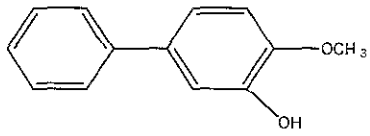
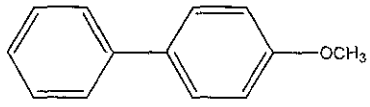
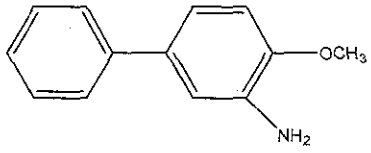
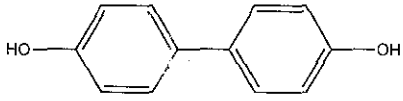
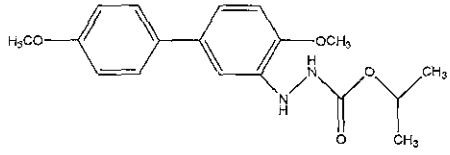
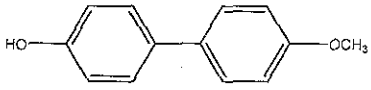
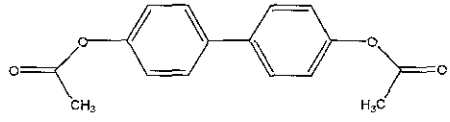
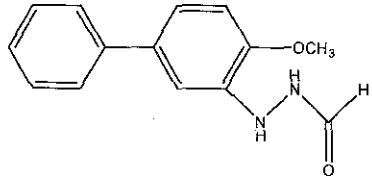
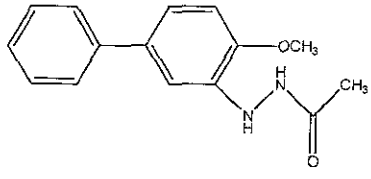
Crop(s)	MRL (mg/kg)	Crop(s)	MRL (mg/kg)

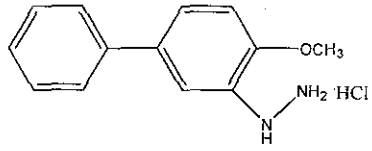
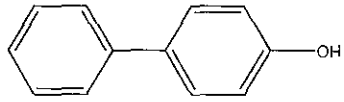
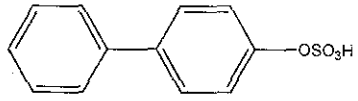
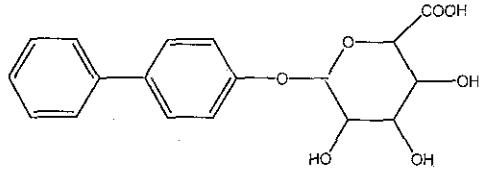
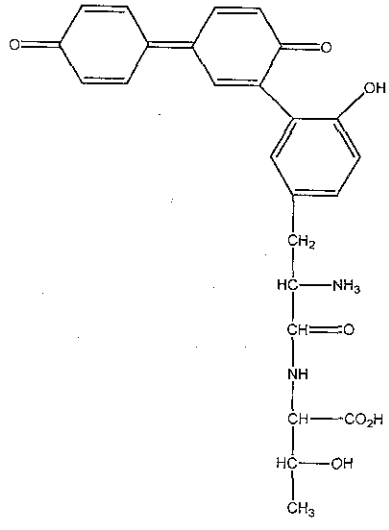
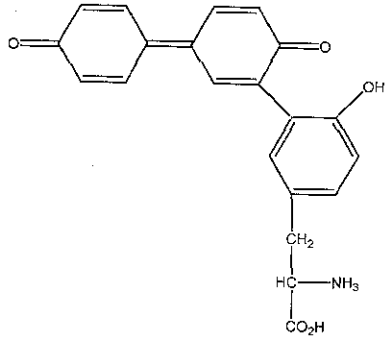
Notes/Special Instructions:
S.Funk, 01/08/01

Rev. 1998

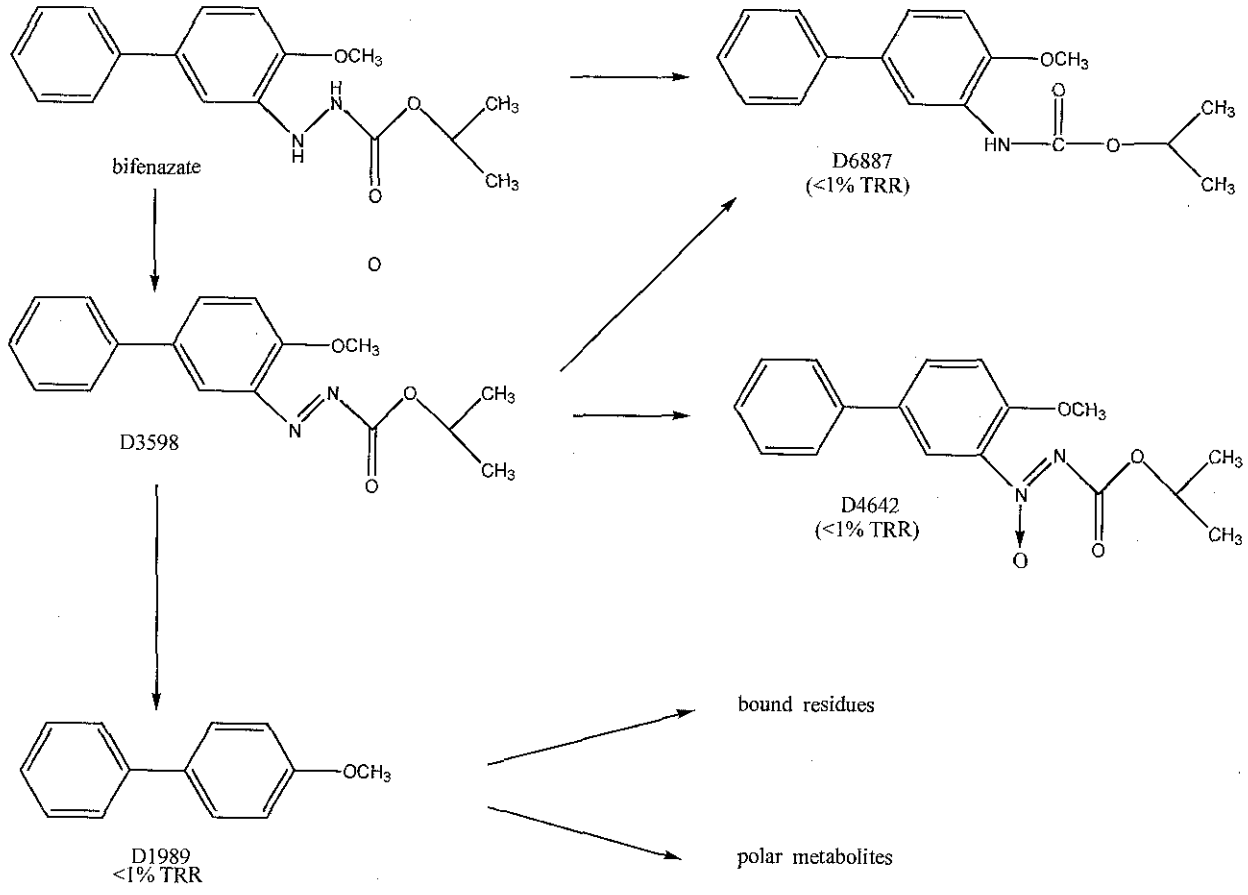
attachment 2: chemical structures

chemical name	chemical structure
bifenazate (D2341) hydrazinecarboxylic acid, 2-(4-methoxy-[1,1'-biphenyl]-3-yl), 1-methylethyl ester	
D2341-glucuronide	
D3598 diazinecarboxylic acid, 2-(4-methoxy-[1,1'-biphenyl]-3-yl), 1-methylethyl ester	
D4642 diazinecarboxylic acid, 2-(4-methoxy-[1,1'-biphenyl]-3-yl), 1-methylethyl ester 2-oxide	
D6887 carbamic acid, (4-methoxy-1,1'biphenyl]-3-yl)-, 1-methylethyl ester	
D4274 [1,1'-biphenyl]-4-ol, 3-amino	
D9472 [1,1'-biphenyl]-3,4-diol	

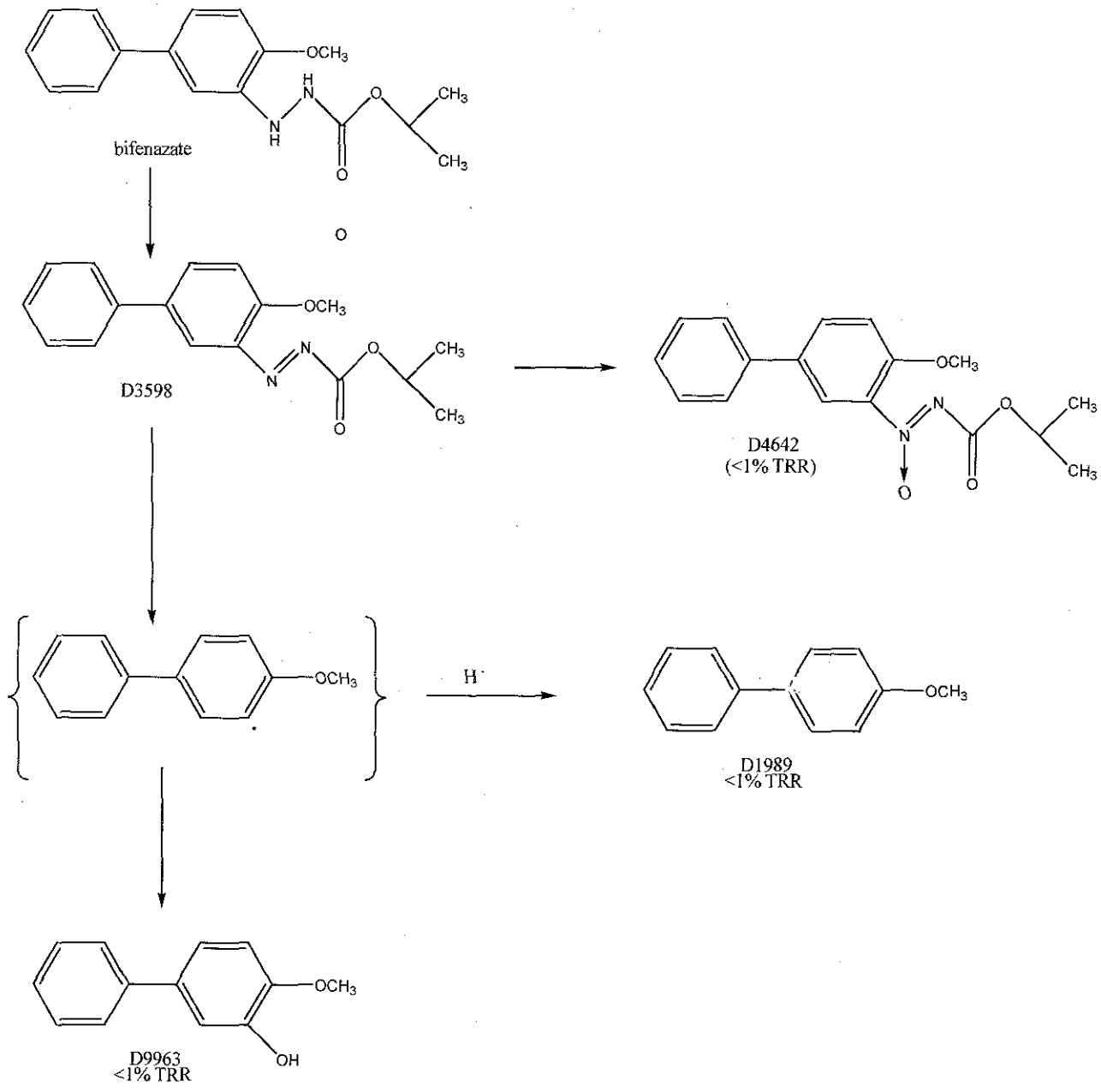
chemical name	chemical structure
D9963 4-methoxy-[1,1'-biphenyl]-3-ol	
D1989 1,1'-biphenyl, 4-methoxy	
D4111 [1,1'-biphenyl]-3-amine, 4-methoxy	
D9569 [1,1'-biphenyl]-4,4'-diol	
D8654 hydrazinecarboxylic acid, 2-(4,4'-dimethoxy-[1,1'-biphenyl]-3-yl)-, 1-methylethylester	
D9477 [1,1'-biphenyl]-3-ol, 4-methoxy	
D9474 [1,1'-biphenyl]-4,4'-diol, diacetate	
C8932 hydrazinecarboxaldehyde, 2-(4-methoxy-[1,1'-biphenyl]-3-yl)	
C8935 acetic acid, 2-(4-methoxy-[1,1'-biphenyl]-3-yl)-, hydrazide	

chemical name	chemical structure
I0199 hydrazine, (4-methoxy-[1,1'biphenyl]-3-yl-, hydrochloride	
A1530 1,1'-biphenyl, 4-ol	
A1530-sulfate	
A1530-glucuronide	
threonyl-tyrosine adduct of oxidized D9569	
tyrosine adduct of oxidized D9569	

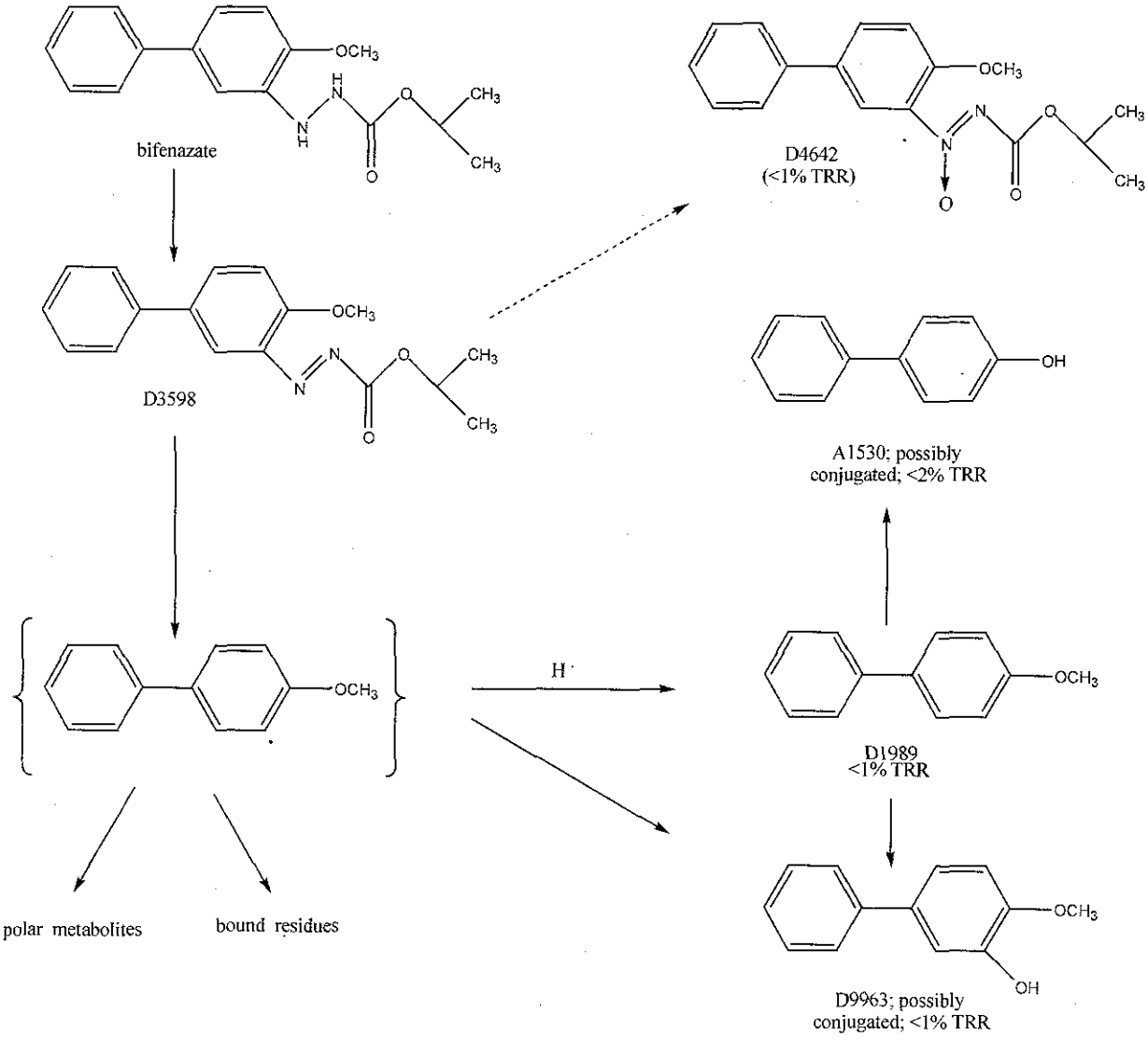
attachment 3: petitioner proposed metabolic pathway in apple



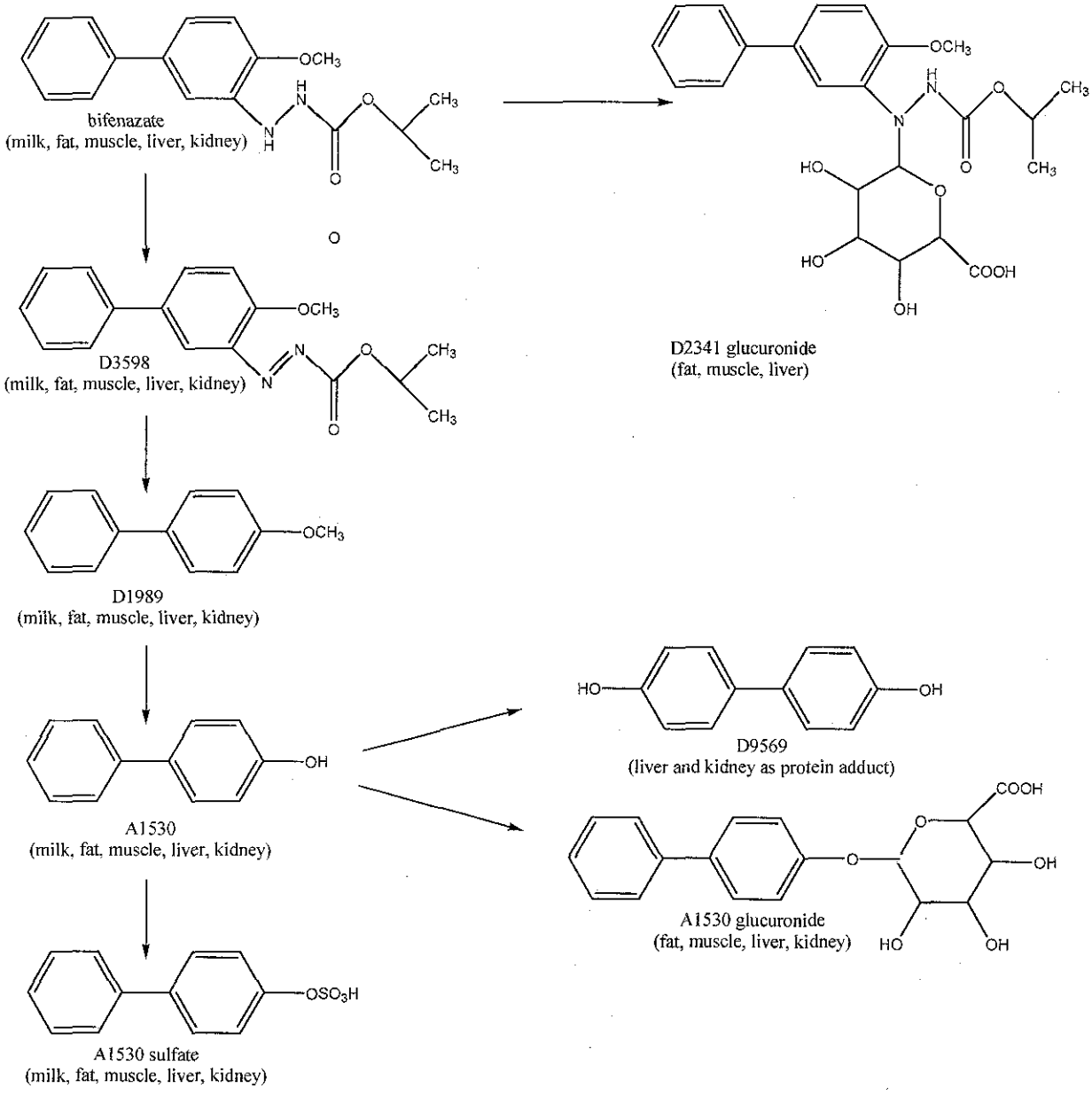
attachment 4: petitioner proposed metabolic pathway in citrus



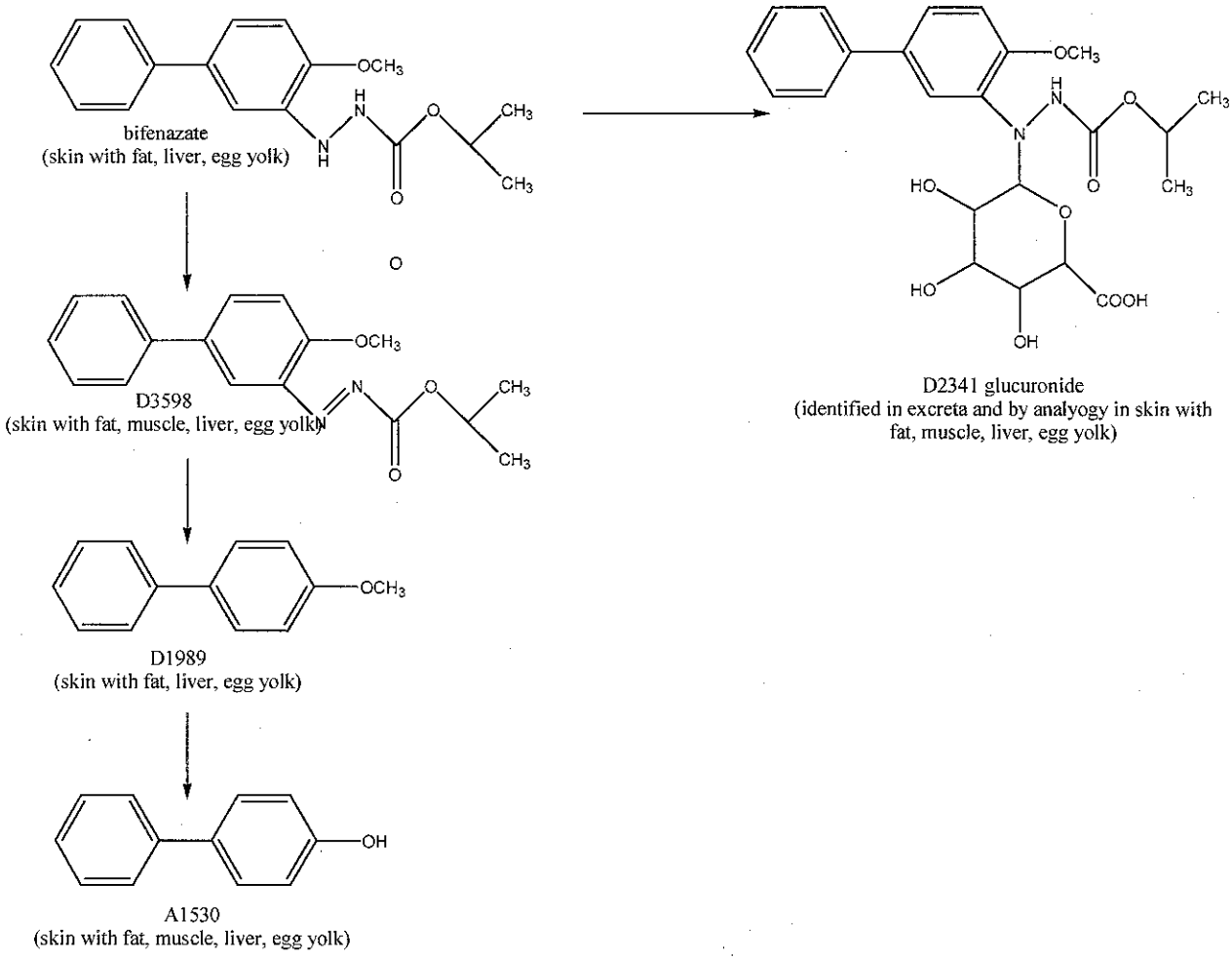
attachment 5: petitioner proposed metabolic pathway in cotton



attachment 6: proposed metabolic pathway in lactating goats



attachment 7: proposed metabolic pathway in laying hens



13544

031879

Chemical:	**Hydrazinecarboxylic acid, 2-(4-methoxy{1**
PC Code:	**000586**
HED File Code	**11000 Chemistry Reviews**
Memo Date:	**08/16/2001**
File ID:	**DPD277089**
Accession Number:	**412-02-0006**

HED Records Reference Center
12/10/2001